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LETTERS TO THE EDITOR

Lung structure and function in cigarette smokers

In their paper (May 1994;**49**:473–8) Dr Hogg and colleagues are to be congratulated on the size of their lung collection from which they conclude that neither lesions in the bronchioles nor emphysema are related to the forced expiratory volume in the first second as a percentage of predicted (FEV_1%). This is so at variance with the large body of literature that has accumulated over the past 30 years that their data require critical examination.

In their study surgically resected specimens were used for lung cancer, introducing the variable of an effect of tumour. The cases used have been described in the past as "coin lesions" or "isolated lesions" but it would be more useful to describe the actual staging. If these tumours are all T_1N_0 then the direct effect of the tumour must be regarded as small; if other stages are present this may not be the case, and readers should be given the opportunity to assess the quality of this large collection. The bulk of these cases are lobectomies (only 8·8% of the right lung specimens are from pneumonectomy; 23·7% of left lungs). In the remaining cases the lobes (including 17 middle lobes) have to be projected to the whole lung for assessment of bronchiolar inflammatory lesions (Cosio score), average interalveolar wall distance (LM), alveolar attachments, and emphysema. In the case of the Cosio score, the effect of lobe selection is controversial[1–4] and a thorough and careful analysis is not yet available. Alveolar attachments were lower in upper lobes[4] as would be expected since emphysema is dominantly an upper zone disease. Dr Hogg and colleagues have used a "modification" of the panel grading method[5] that we designed to assess emphysema in whole lung, paper-mounted sections in epidemiological surveys. It was not meant to assess emphysema in slices of formalin fixed lobes. It is indeed possible to *guess* at how much emphysema there is in a whole lung from a slice of formalin fixed upper lobe since the panel system shows emphysema at all scores between 5 and 25. However, the lower lobe panels do not have emphysema so that the guess from lower lobe to whole lung can only be regarded as hazardous. This is not a trivial problem since the emphysema score for all of the cases in the paper by Hogg *et al* can be calculated and averages 9·8. Their results show a lower score than others using similar cases in the same city[6] and the reason for this is not apparent. Their reported incidence of emphysema is 39·6% while others have reported figures from 49% to 100%, typically 70–80%.[6–10]

Another necessary projection is to lung volume at TLC so that LM (an approximation of interalveolar wall distance) can be measured. This correction is important since the interalveolar wall distance depends on the degree of inflation. The precise way the correction was achieved is not described, but from another paper in their laboratory[11] it would appear that the amount of fixative in the appropriate lobes was compared with TLC, assuming that the right and left lower lobes each contributed 35%, the middle lobe 5%, and upper lower lobe 15% (total 105%). Because of these gross approximations it was probably not worthwhile attempting to correct for the volume of air in the fixed lung and the volume of fixed lung. However it was done, it would appear that it was not successful as the LM measurement was about half that usually found and cannot be ascribed to "the higher magnification" at which the measurement was made, as suggested by Hogg *et al.* Even electron microscopy only increases alveolar surface area by about 50%.

Dr Hogg and colleagues make the point that the Cosio score[12] of bronchiolar lesions is a sum of eight variables, and that an abnormal score does not identify which variable(s) has/have contributed to flow obstruction. This point is well taken, but the Cosio score does not include a measurement of airway narrowing for which there is abundant evidence that it contributes to airflow obstruction. In addition, deformity[13] or "ellipticality"[14] of airways has been shown to be related to flow obstruction and these two important topics are not addressed in Dr Hogg's paper.

Perhaps most importantly, table 2 in the paper by Hogg *et al* may be misinterpreted by casual readers. This table indicates that the emphysema score is much the same in all categories of FEV_1%. However, the score refers *only* to the mean of those lungs recognised by them as having emphysema. When the average emphysema scores of all lungs in each FEV_1% category is calculated one finds a steady increase in emphysema with the fall in FEV_1%.

The figure in their paper deserves comment because of the statement that "10 of 54 patients with FEV >100% predicted had emphysema of similar severity". The specimen shows severe localised subpleural emphysema that one would expect to be associated with spontaneous pneumothorax and *not* with airflow obstruction. The bulk of the specimen is free from emphysema and, indeed, shows what appears to be patchy obstructive pneumonitis.

The only substantiation from the literature quoted by Hogg *et al* for their view that "the extent and severity of these lesions . . . (grossly visible emphysema) . . . was similar at all levels of FEV_1" is the paper by Gelb *et al*,[15] already criticised by Snider without adequate rebuttal to the authors.[16] Gelb's conclusion was based on CT scanning which may underestimate the incidence of morphological emphysema by some 18% even when surgical lungs are used, and when CT slices are compared with exactly the same slice in the specimen the emphysema severity is underestimated by a factor of about three.[6]

Finally, the conclusion is reached that "loss of recoil is better explained by a microscopic increase in airspace size than by gross emphysematous destruction". I assume that Dr Hogg means that LM is better related to elastic properties of the lung than emphysema. I agree that emphysema and elastic properties are poorly related,[17] but "better" in this context is a relative term. It might be more accurately stated that, according to data from their laboratory, elastic properties of the lung are about as badly related to LM as to emphysema.[11 17] Incidentally, LM is not a measurement of alveolar size – this deceptively simple measurement reflects also the size of the alveolar duct (as defined in a particular way) as well as all the tissue in which LM is measured. It is thus not true to state, as Dr Hogg does on page 470 of the paper, that "the decline in lung function is associated with microscopic evidence of enlarged alveolar size".

This paper not only provides no answers but raises many more questions that require answers. In my view chronic airflow obstruction is a complicated matter in which different lesions of bronchi (not just "chronic bronchitis"), bronchioles (not just the Cosio score), and parenchyma (not just emphysema) contribute. In any one patient these lesions occur with different degrees of severity, are recognised by investigators with varying degrees of precision, are reported in different ways with different insights, and it is exceedingly rare that any single lesion can be considered to be of overwhelming importance.

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1 Cosio MG, Hale KH, Niewochner DE. Morphologic and morphometric effects of prolonged cigarette smoking on the small airways. *Am Rev Respir Dis* 1980;**122**:265–71.
2 Berend N. Lobar distribution of bronchiolar inflammation in emphysema. *Am Rev Respir Dis* 1981;**124**:218–20.
3 Wright JL, Wiggs BJ, Hogg JC. Airway disease in upper and lower lobes of patients with and without emphysema. *Thorax* 1984;**39**:282–5.
4 Willems LNA, Kramps JA, Stijnen T, Sterk PJ, Weening JJ, Dijkman JH. Relationship between small airway disease and parenchymal destruction in surgical lung specimens. *Thorax* 1990;**45**:89–94.
5 Thurlbeck WM, Dunnill MS, Hartung W, Heard BE, Heppleston AG, Ryder RC. A comparison of three methods of measuring emphysema. *Hum Pathol* 1970;1:215–26.
6 Miller RR, Müller N, Vidal S, Morrison NJ, Staples CA. Limitation of computed tomography in the assessment of emphysema. *Am Rev Respir Dis* 1989;**139**:980–3.
7 Kuwano K, Matsuba K, Ikeda T, Murakami J, Araki A, Nishatani H, *et al.* The diagnosis of mild emphysema. Correlation of computed tomography and pathology scores. *Am Rev Respir Dis* 1990;**141**:169–78.
8 Gillooly M, Lamb D. Microscopic emphysema in relation to age and smoking habit. *Thorax* 1993;**48**:491–5.
9 Morrison NJ, Abboud RT, Müller NL, *et al.* Pulmonary capillary blood volume in emphysema. *Am Rev Respir Dis* 1990;**141**:53–61.
10 Berend N, Woolcock AJ, Marlin GE. Correlation between the function and structure of the lung in smokers. *Am Rev Respir Dis* 1979;**119**:695–705.
11 Osborne S, Hogg JC, Wright JL, Coppin C, Pare PD. Exponential analysis of the pressure-volume curve. Correlation of mean linear intercept and emphysema in human lungs. *Am Rev Respir Dis* 1988;**137**:1083–8.
12 Cosio M, Ghezzo M, Hogg JC, Corbin R, Loveland M, Dosman J, *et al.* The relations between structural changes in small airways and pulmonary-function tests. *N Engl J Med* 1978;**298**:1277–81.
13 Nagai A, West WW, Thurlbeck WM. The National Institutes of Health intermittent positive pressure breathing trial: pathology studies II. Correlation between morphologic findings, clinical findings and evidence of expiratory airflow obstruction. *Am Rev Respir Dis* 1985;**132**:946–53.
14 Lamb D, McLean A, Gillooly N, Warren PM, Gould GA, MacNee W. Relationship between distal airspace size, bronchiolar attachments, and lung function. *Thorax* 1993;**48**:1012–7.
15 Gelb AF, Schein M, Kuei J, Tashkin DP, Müller N, Hogg JC, *et al.* Limited contribution of emphysema in advanced chronic obstructive pulmonary disease. *Am Rev Respir Dis* 1993;**147**:1157–61.
16 Snider GL. CT and COPD (correspondence). *Am Rev Respir Dis* 1994;**149**:552.
17 Thurlbeck WM. Christie lecture: Emphysema then and now. *Can Respir J* 1994;**1**:21–39.