There is a group of chest diseases in which dyspnoea is associated with limitation of expiratory airflow and it is to the treatment of this impaired airflow that therapy is mainly directed and to which the drug industry devotes much attention.

Implicit in this attitude is the assumption that the characterising feature of the group of diseases is similar and that it is only limitation of expiratory airflow. In addition there is a defect of gas mixing, and the conventional explanation is that it results from a failure of gas distribution by the airways. There is also a further assumption, which is that the process of gas mixing by diffusion within the terminal ventilatory unit is complete within the time of a respiratory cycle.

So we have a unitary hypothesis which explains both airflow limitation and gas mixing by the same mechanism and this represents the conventional wisdom.

It follows from this hypothesis that the more severe the airflow limitation, then the greater must be the defect in gas mixing so that measures of both in a series of patients would show a good correlation. Such a study carried out in my laboratory is shown in Fig. 1, where FEV₁₀ is used as a measure of airflow limitation and alveolar mixing efficiency for nitrogen is also plotted. As you see the correlation is poor, and the correlation coefficient calculated was 0.06.

This observation denies the conventional unitary hypothesis and suggests that airflow limitation and gas mixing are independent variables. Since this is so a new hypothesis for the genesis of impaired
mixing is called for, and this hypothesis must not involve the function of large airways.

It is possible therefore:

(a) that it is concerned with the small airways and
(b) that it is concerned with the assumption made in the unitary hypothesis that gas mixing by diffusion is complete within one respiratory cycle.

Understanding the process of gas mixing is made easier by considering the situation which obtains when a subject inspires pure oxygen and the nitrogen concentration in the expirate is measured, giving a trace such as is shown in Fig. 2(a) in which expired nitrogen concentration is plotted against expired volume. From such a trace the slope of the plateau can be measured and an increase in this slope has been used for clinical diagnostic purposes and the explanation for its origin has used regional ventilation as its basis.

More information can be obtained from the same data if the quantity of nitrogen expired is calculated. Figure 2(b) indicates that expired flow is measured at the same time as expired concentration. The two curves are sampled by a computer as indicated in Figure 2(a) and (b), and each value of concentration is multiplied by each value of flow, the product indicating the quantity of nitrogen evolved during the short sampling period.