ALTERED PULMONARY FUNCTION IN BRONCHIAL ASTHMA

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Asthma has attracted a great deal of attention over the centuries both because it is common and because of its frequent dramatic manner of presentation (Ellul-Micallef, 1976). Up to comparatively recently, knowledge of physiological changes occurring in asthmatic patients, both during an attack and following therapy has been scanty. Over the past few years various tests have been developed enabling the clinical pulmonary physiologist and the chest physician to measure a number of different variables. It is only by considering all the changes in pulmonary function which take place in this condition that a reasonably clear picture can be obtained and a rational approach to therapy instituted. In this article discussion of altered pulmonary function in asthma includes changes in:

(i) Airway resistance.
(ii) Lung volumes.
(iii) Lung elastic recoil pressure.
(iv) Pulmonary diffusing capacity.
(v) Arterial blood gas tensions and pulmonary gas exchange.

(i) Airway resistance in asthma

Increased and variable airway resistance may be said to be the physiological hallmark of bronchial asthma. In general the forced expired volume in one second (FEV_1), the maximum mid-expiratory flow rate (MMFR) and the peak expiratory flow rate (PEFR) are found to be decreased from the predicted values and are likely to be related to the severity of symptoms. The ratio of the forced expired volume in one second to the forced vital capacity is also found to be reduced. Subjective improvement in the patient's condition is not always reflected in a proportional change in these tests. Clinical improvement may occur while some spirometric tests such as the FEV_1, remain unaltered. The improvement may be reflected by a decrease in lung volumes (Woolcock & Read 1966; Weng and Levinson, 1969).

Airway resistance (Raw) as measured by body plethysmography is believed to provide a direct measurement of the resistance to the flow of air. The Raw is always increased, frequently very considerably, and the specific conductance (SGaw), that is, the conductance divided by the thoracic gas volume at which the airway resistance is measured, correspondingly decreased during the acute phase, both indices returning towards normal values as the patient's condition improves (Lapp Le Roy and Hyatt 1697; McFadden & Lyons 1968, 1969; Pelzer & Thomson 1969; Fisher et al 1970; Daly 1971). An increased Raw has also been found in some symptom free asthmatic patients (Ruth & Andrews 1959; Bernstein & Kreindler 1963). Cade et al (1971) provoked bronchoconstriction in symptom free asthmatic subjects with nebulized metacholine. They found that pulmonary resistance increased within one breath of the metacholine inhalation and was the measurement of lung function which changed most in response to drug when it was compared with changes in FEV_1 and lung volumes obtained by helium dilution. Airway resistance is of course also increased in chronic bronchial asthma; it has been shown to decrease on corticosteroid adminitration (Ellul-Micallef et al, 1971, 1972, 1974).

(ii) Lung Volumes

The vital capacity is generally decreased in asthma and is usually more severely

diminished the greater the degree of airway obstruction. A decrease in vital capacity commonly persists during the symptom free phase of bronchial asthma (Levine et al 1970). Lowell et al (1955) used the vital capacity to follow changes in asthmatic patients, but it proved to be a less sensitive index than the dynamic ventilatory tests. A number of reports have appeared in which measurements of the total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV) in asthmatics were found to be elevated, thus reflecting the presence of a certain degree of hyperinflation. A reversible increase in TLC was first documented in asthma as early as 1934, when Hurtado and Kaltreider observed a decrease in TLC following the administration of adrenaline to patients with acute asthma. Since then a considerable number of papers reporting the changes in lung volumes that occur during acute asthma and the period of recovery have been published (Woolcock and Read, 1965; 1966; 1968; Meissner and Hugh-Jones 1968; Weng and Levison 1969; Palmer and Diament 1969; Stanescu and Tetulescu 1970; Mayfield et al, 1971; Freedman et al, 1975). Lung volumes have also been reported to be elevated in chronic asthma returning towards predicted normal values after corticosteroid therapy (Ellul-Micallef et al 1971, 1974).

In general, the more severe the degree of airway obstruction the greater the amount of hyperinflation present, shown by an elevated TLC, FRC and RV; all indices tending to decrease following successful treatment. In some of the patients reported by Woolcock and Read (1965) the FRC during acute asthma was greater than the TLC after recovery. In these patients tidal breathing during severe obstruction must have been taking place at a higher level than the point of maximal inspiration after recovery. Mead, Milic-Emili and Turner (1963) claim that inhibiting reflexes normally limit the degree of voluntary lung inflation; if this is true, then one must presume that such reflexes are modified in asthma. Palmer and Diament (1969) similarly found that in asthma as the airway obstruction increased there is a progressive hyperinflation of the lung and that when the obstruction is reduced by a bronchodilator, hyperinflation becomes less. Of the indices of hyperinflation they found that only RV/TLC% correlated consistently with the dynamic lung volumes and regard it as the best single measurement of hyperinflation in this condition.

Various studies have now been reported in which serial measurements of FRC by a helium dilution method and thoracic gas volume by body plethysmography have been carried out in asthmatics during the acute attack and the subsequent recovery period (Meisner and Hugh-Jones 1968; Stanescu and Teculescu 1970). In general, plethysmography yielded signficantly larger FRC values than did the helium method. The differences were greatest when the asthma was most severe and decreased during clinical recovery. As the helium dilution method reflects the volume of ventilating parts of the lung, there appear to be portions of the lung which fail to ventilate during the time involved in helium equilibration.

Hyperinflation may persist in the asthmatic patient even in the symptom free phase (Beale et al 1952; Gold et al 1967; Levine et al 1970). An increase in FRC may be compensatory to the decreased bronchial calibre found in asthma and to a certain extent this may have a guy-rope effect in helping to maintain the patency of the airways. This is not obtained without a disadvantage to the patient, for as the lung volume increases, compliance diminishes progressively so that the further inhalation of a given volume of air requires the production of a higher transpulmonary pressure difference because the patient is breathing on a flatter part of the Pressure-Volume (P-V) curve. The elastic work of inspiration will be greatly increased and presumably must make considerable contribution to the patient's sensation of dyspnoea. Asthmatic patients thus often find as much difficulty with inspiration as with expiration.

(iii) The Lung elastic recoil pressure in Asthma

In 1963, in two separate studies, Macklem and Becklake, and Ting and Williams both reported mean inspiratory static pressure-volume (P-V) curves in normal subjects, in patients with asthma and in those with emphysema. In both studies the P-V curves for symptom free asthmatics were shifted upwards and to the left as compared with the mean curve for normal subjects; i.e. it appeared that the lung elastic recol pressure, Pst(l), was reduced. Macklem and Becklake (1963) corrected for the increased lung volume seen in some of their subjects by calculating the "over-all compliance' (Mead et al 1955), i.e. the ratio of TLC to the maximum negative intrapleural pressure. This correction reduced the difference between the normal group and the group of asthmatics but accentuated the loss of elastic recoil in the group with emphysema. Work by Tooley and his associates (1965) provides supporting evidence.

Several workers have since measured Pst(l) in asthmatics both during exacerbations as well as in symptom free phases to try and establish whether it is indeed reduced in asthma (Gold, Kaufman and Nadel 1967; Woolcock and Read 1968; Finucane and Colebatch 1969). Gold and his associates showed that the Pst(l) was decreased at all lung volumes in seven of their twelve asthmatic subjects. After a week's treatment with corticosteroids and bronchodilators, the increase in airway resistance and in lung volume reverted to normal and their P-V curves moved back to the normal range, in all the patients but one. In the latter, a further week of treatment finally reversed all abnormalities. Gold also induced bronchoconstriction in four asthmatics who had normal P-V curves and in one normal subject, with a 0.03% histamine phosphate inhalation. Although this resulted in a mean airway resistance of 320% of the pre-inhalation value, the Pst(l) remained normal. Acute hyperinflation of the chest in a normal subject for an hour also resulted in insignificant changes in Pst(l). It thus appears that loss of lung elastic recoil pressure is slow to develop. Woolcock and Read (1968), reported a decreased Pst(l) in six out of their ten asthmatic subjects, during an exacerbation of symptoms. Unlike Gold's patients, after intensive therapy, although the airway resistance returned to normal in almost all the patients, the loss of lung elastic recoil and hyperinflation persisted in five subjects.

Finuncane and Colebatch (1969) assessed the elastic properties of the lung in patients with asthma, emphysema and in normals, by measuring the static P-V curves of the lung during deflation from TLC after a standard volume history. The P-V characteristics of this study thus reflect mainly the elastic properties of lung tissue since the pulmonary retractive pressure was measured during deflation from TLC when lung surface forces contribute least (Radford, 1946) In three of the four asthmatic patients studied there was a persistent reduction of pulmonary elastic recoil pressure despite relief of airway obstruction for six weeks or longer. This finding agrees with that of Woolcock and Read (1968) and it seems likely that some patients with severe asthma might have a more or less permanent reduction of Pst(l).

The cause of the loss of elastic recoil of the lungs in asthmatic subjects is unknown. According to Mead (1961), the static P-V curve is dependent on two factors: the tension exerted by surfactant and the elastic properties of pulmonary tissue. The tissue component of the elastic retraction of the lung resides in the close association and architectural arrangement of collagen and elastin fibres in the respiratory bronchioles, alveolar ducts and alveoli (Pierce and Ebert 1969). In emphysema this fibre network is disrupted (Wright 1961) and elastic retraction of the lung would be expected to be and is in fact reduced. In asthma the fibre network is intact (Gough 1955) and hence other factors must be responsible for the loss of elastic recoil. Gold et al (1967) have suggested that prolonged distension of the connective tissue of the lungs causing temporary structural deformation is a

possible explanation. Other alternatives that must be considered are that the changes could be related to the forces exerted by surfactant; or the changes may be due indirectly to a reduction in perfusion to some alveoli, which affects their producton of surfactant or of another product important to the normal retractile forces.

Finucane and Colebatch (1969) suggested that the loss of elastic recoil could be the result of a reduction of tissue forces due to tissue stress-relaxation (Marshall & Wi dicombe, 1961). In asthma, stress-relaxation may occur in those parts of the lung held inflated by airway closure. Theoretically, the reduced retractive pressure in asthma could also involve increased recruitment of surface active molecules consequent upon prolonged over-expansion of the lung (Tierney & Johnson 1965). It is known that the surface tension of a liquid is inversely related to the concentration of surface-active molecules in the surface (Davies & Rideal 1961).

Woolcock and Read (1969) suggested that hyperinflation of the lung, may itself, cause a reduction in lung elastic recoil in a manner in which they could not explain fully. They looked at the problem from the opposite point of view from that of Gold and his associates. The latter considered the loss of elastic recoil to be responsible for the hyperinflation in asthma. If hyperinflation of the lungs itself causes a reduction in elastic recoil, then a residual abnormality in the airways sufficient to maintain a degree of hyperinflation could account for the apparent loss of lung elasticity in symptom free asthmatics. This could possibly account for the differences in results reported by Gold et al (1967) and Woolcock and Read (1968). All the patients reported on by Gold and his coworkers had normal lung volumes when the lung elastic recoil was measured after a week's therapy, whilst those reported on in the other two studies had persistent hyperinflation.

In a recent paper, Peress et al (1976) reported findings which indicate that the increase in Total Lung Capacity in acute asthma results from a combination of loss of lung elastic recoil, increased outward recoil of the chest wall and increased strength of contraction of the inspiratory muscles. They suggest that this may be the result of a rapid change in the elastic properties of lung and chest wall. Such properties have up to now been regarded as fixed and immutable.

(iv) The pulmonary diffusing capacity in Asthma

The measurement of the pulmonary diffusing capacity (DLco) in asthma has produced discordant results. Some workers have claimed that diffusing capacity values remain remarkably normal but others have shown that a considerable reduction may be present. Among the first to report normal values were Bates (1958) and Macklem and Becklake (1960) who used a steady state method to measure DLco Macklem and Becklake reported that both DLco and elastic recoil were well preserved in asthma and contrasted this with the decrease in both variables that occurred in the emphysematous patients they studied. They found, that at equivalent values of pulmonary conductance, emphysema is characterized by a considerably lower DLco than asthma. Normal values for diffusing capacity have also been reported when this was measured by the single breath method (Burrows et al 1961; Kanagami et al 1961; McFadden and Lyons 1968: Meissner and Hugh-Jones 1968; Daly 1971). The diffusing capacity was found to be normal even when the FEV_1 was markedly decreased (Bedell and Ostiguy 1967; McFadden and Lyons 1968; Ogilvie 1968; Meissner and Hugh-Jones 1968).

On the other hand, Palmer and Diament (1969, 1970) using the single breath method measured the diffusing capacity in all grades of severity of asthma and found that it fell signficantly as the degree of asthma became more severe. They reported a mean value for DLco of 16.2 + 7.3 ml/min/mmHg when the FEV% was less than 40% (the predicted being 26.1 ± 2.70 ml/min/mmHg); this value improved when salbutamol was administered. Weng and Levinson (1969) measured the diffus-

ing capacity by the steady state method in thirty asthmatic children during an acute attack and repeated the measurements when they were in a symptom-free status. They found that it was significantly reduced during an acute attack but returned to the normal range during the symptom free period. The indices DLco/TLC and DLco/FRC which were markedly reduced during the attack remained significantly lower than normal during the symptom free period. These findings have been supported by the work of Levine et al (1970) who using a steady state method report a lower than predicted value in a group of six symptom free asthmatcs.

Pecora, Bernstein and Feldman (1966) measured the diffusing capacity by the single method in twenty six children with intractable asthma. They reported that in sixteen children with hyperinflated lungs the diffusing capacity was greater than predicted, whilst in the ten children who had no pulmonary hyperinflation the diffusing capacity was normal. They suggested that this increase is due to a moderate increase in surface area of the lung and a greater decrease in the thickness of the alveolar membrane. Ogilvie (1968), too, reports higher than predicted values in a number of asthmatics, and points out that an imbalance between ventilation and perfusion can sometimes result in erroneously high values.

Forster (1957) in his classical review of the processes of pulmonary diffusion and their assessment refers to the errors which may be introduced by non-uniformity of various variables. Although the concept of a diffusing capacity is not a difficult one to envisage, the details of its measurement and the interpretation of the results obtained by the various techniques are far from straightforward, especially in clinical conditions in which there is inhomogeneous distribution of alveolar gas. Bates, Macklem and Christie (1971) have ascribed the difficulty in sorting out the apparent discrepancy of the diffusing capacity values in asthma obtained by various workers to four main factors — patient selection, variation in degree of airway obstruction, differences in technique and the uncertain interpretation of results obtained from induced bronchoconstriction. Difficulty often arises, when selecting patients, in differentiating between those suffering from asthma and those with chronic bronchitis with a degree of emphysema.

However, the interpretation of reports on diffusing capacity in bronchial asthma is perhaps most seriously hampered by the variety of methods used in its determination. It is obvious that each method measures something different and probably none measures the true diffusing capacity of the 'pulmonary membrane'. The accuracy of each method for measuring this index of pulmonary function depends on certain critical assumptions about the relative uniformity of blood flow, ventilation and alveolar volume and if one of these assumptions is incorrect the measurement becomes biased. Since the assumptions are different for each method of measurement, a given type of non-uniformity in the lung is bound to bias the diffusing capacity measured by one method more than by another. This possibly accounts for most of the discrepancy between the various reports. Ohman et al (1972) measured the diffusing capacity in ten symptomatic asthmatics by both the single breath and steady state methods before and after treatment. The diffusing capacity measured by the single breath method was greater than predicted on both occasions. The mean pre-treatment value obtained by the steady state method was 51% of the predicted and it went up to 66% of the predicted following therapy.

The severity of the disease during which the measurement is made is another important factor to keep in mind when assessing results. Tests of diffusing capacity must be to a greater or lesser extent influenced by ventilation-perfusion abnormalities (Apthorp and Marshall 1961). Thus although the single breath method is said to be less sensitive to ventilation-perfusion (V/Q) abnormalities, in severe cases an impaired distribution of inspired air, regional V/Q variations and the DI/Q ratio can decrease the value of the transfer factor obtained by the single breath method

(Piiper and Sikand 1966). The transfer of gas in bronchial asthma thus appears to be more impeded by failure to deliver inspired gas to the alveolar surface than by interference with diffusion through the 'pulmonary membrane'.

(v) Arterial blood gas tensions and pulmonary gas exchange.

Very little attention was paid to the changes that occur in blood gases during asthma until comparatively recently. Bates and Christie (1964) stated that, "the patient with moderately severe bronchospasm but not in status asthmaticus only rarely shows any significant abnormality of arterial oxygen saturation or CO_2 tension". It had been generally assumed that the $PaCO_2$ is usually normal or low, due to hyperventilation until the terminal stages of status asthmaticus, when the $PaCO_2$ rises rapidly and respiratory failure supervenes (Marchand and van Hasselt 1966). Before the important paper of Tai and Read in 1967 there had only been occasional reports of blood gas disturbances in bronchial asthma (Herschfus et al 1953; Williams and Zohman 1960; Feldman 1962).

Tai and Read (1967) were the first to report carbon dioxide retention and marked respiratory acidosis in twelve patients admitted to their care in status asthmaticus. Their data showed that in other patients with only moderate clinical severity considerable hypoxaemia could also be present. Similar results have now been reported by a number of different workers (Rees, Miller and Donald 1968; McFadden and Lyons 1968; Meissner and Hugh-Jones 1968; Miyamoto et al 1970; Rebuck and Read 1971). Arterial PO_2 levels belows 60 mmHg may be associated with PCO_2 levels varying between 30 and 80 mmHg; such a level of PaO_2 is commonly seen when airway obstruction is severe, with an FEV_1 below 30% of the predicted normal value.

Flenley (1971) states that if milder cases are included the fall in PaO_2 seems to bear a roughly linear relation to the FEV_1; normal PaO_2 values being usual when the FEV_1 is above 2 litres. Tai and Read (1967) found a general correlation between the degree of reduction of the FEV_1 and the extent of disturbance of blood gas tensions in their study of sixty four patients with moderately severe asthma. They pointed out that FEV_1 levels of less than a litre were especially associated with a significant reduction of arterial PO_2. However, it should be stressed that the correlation is not good enough to make FEV_1 levels greater than a litre a reliable index of a fairly normal arterial oxygen tension. Palmer and Diament (1968, 1969) reported a correlation between PaO_2 and the RV/TLC%, hypoxaemia becoming progressively more severe as hyperinflation develops.

Rees, Millar and Donald (1968) following the clinical course and arterial blood gas tensions of twenty four patients in status asthmaticus, found that hypoxaemia was invariably present, was frequently quite marked and persisted despite extensive therapy sometimes for weeks. Most patients were normocapnic or even hypocapnic. When severe hypercapnia was present the patients generally died. They found that changes in $PaCO_2$ were inversely related to changes in pH, and patients with severe hypercapnia also had metabolic acidosis. The pulse rate correlated well with PaO_2 and in the severely hypoxaemic patients the frequency exceeded 130 beats/min. McFadden and Lyons (1968) studied ninety one patients during an acute asthmatic attack. All their patients had hypoxaemia but hypercapnia was only present in eleven patients, and was not found till the FEV_1 fell to below 20% of the predicted value. Hence despite the fact that CO_2 retention is a prominent feature in some asthmatics with marked airway obstruction, low PCO_2 values indicating hyperventilation are frequently encountered. Hypocapnia and respiratory alkalosis was present in about 80% of the patients studied by McFadden and Lyons. These studies have now established the fact that hypoxaemia, often of a dangerous degree may be present in asthmatic patients, and that severe hypercapnia is not usually present except terminally. Feldman (1962) pointed out the grave prognostic signifi-

cance of an increase in $PaCO_2$ in adults with severe asthma.

The accompanying disturbance in the acid-base balance as reflected in the arterial blood, shows that the hypercapnia in most of these patients probably develops acutely. Flenley (1971) analysing the data from various authors (Mithoefer et al 1968; Tabb and Guerrant 1968; Tai and Read 1967; Downes et al 1968; Simpson et al 1968) concluded that chronic elevation of PCO_2 is relatively uncommon is asthma. The increased renal reabsorption of bicarbonate which is an important defence against respiratory acidosis would appear to be too slow a mechanism to be of great importance in acute asthma, where dangerous hypercapnia may develop very acutely. Mithoefer et al (1968) have found that correction of the respiratory acidosis by infusion of sodium bicarbonate was valuable in treating intractable asthma, but others seem to have had less success with this approach (Flenley 1971).

Hypoxaemia, with or without CO_2 retention, implies a maldistribution of ventilation and perfusion in the lungs which is shown by increased alveolar — arterial tension differences for oxygen (A-a) DO_2 and higher ratios of physiological dead space to tidal volume (VD/VT). A higher than normal (A-a)DO_2 and VD/VT has been shown to be present both during the acute attack (Field 1967; Meisner and Hugh-Jones 1968; Valabhiji 1968), in chronic asthma (Ellul-Micallef et al, 1972), as well as during the symptom free phase (Levine et al 1970; Waddell et al 1967). Although uneven distribution of pulmonary ventilation in asthma has been recognised for a long time in both the acute phase (Bates 1952; Fowler et al 1952; Herschfus et al 1953; Malmberg et al 1963; Bates et al 1968) and in the symptom free period, (Beale et al 1952), the effect of this on the distribution of pulmonary blood and the ventilation-perfusion relationships had until comparatively recently received less attention. Single cases of asthma with V/Q disturbances had been reported by Donald et al (1952) and by West et al (1957). Ledbetter et al (1964) in a study of asthmatic children reported that an abnormally high percentage of the cardiac output perfused the 'slow' or poorly ventilated compartments in the lungs.

The presence of adaptive mechanisms to divert blood flow away from poorly ventilated regions of the lung were postulated by Barcroft (1930), Anthony (1930), and Haldane (1935). The observation that hypoxia causes an elevation of pulmonary artery pressure probably secondary to pulmonary vasoconstriction led von Euler and Liljestrand (1946) to suggest that pulmonary hypoxia might play a role in controlling the distribution of pulmonary blood flow. Recent work has in general confirmed these suppositions. It is now generally accepted that the concentration of gases in the alveoli determine the resistance to blood flow in the adjacent vessels, and that the chemical stimuli for this local vasomotor control are hypoxia and to a lesser extent acidosis (Liljestrand 1958; Fishman 1961; Fishman 1969). Other workers (Severinghaus and Stupfel 1957; Arborelius 1965) have also shown that a decrease in bronchiolar PCO_2 will redirect ventilation away from poorly perfused areas of the lung.

Although it seems unlikely that local alterations in perfusion could possibly compensate for the unevenness of ventilation in bronchial asthma, there is a lot of evidence to suggest that such homeostatic mechanisms do exist in asthma, and that they tend to reduce the V/Q defect by decreasing the blood flow of underventilated lung units. Factors disturbing these homeostatic mechanisms would be expected to result in an increased V/Q abnormality. Thus, the administration of oxygen, presumably, by abolishing pulmonary vasoconstriction in hypoxic regions, resulted in a worsening of the ventilation-perfusion imbalance in asthmatics as shown by an increase in the (A-a)DO_2 and VD/VT ratio. Breathing pure oxygen has been shown to have no effect on the pattern of V/Q inequality in normal subjects or in patients with chronic lung disease (Riley, Cournand and Donald 1951; Larson and Severinghaus, 1962; Cole and Bishop, 1963). Such a deterioration occurred not only in the acute phase of their illness

(Field 1967) but also in the symptom free period (Valabhji 1968); suggesting that during the latter phase a compensatory reduction of blood flow to underventilated parts of the lung might still be present. Supporting evidence for the existence of pulmonary vasocontriction in asthmatics when symptom free has been produced by Irnell and Noredgren (1966) who infused acetylcholine into the pulmonary artery of nineteen asthmatics and observed a reduction in arterial oxygen saturation in all but one. Valabhji (1968) reports a very small contribution of veno-arterial shunt of 3.7 $\pm$ 1.4% to the hypoxaemia present in their acute asthmatic patients. This is perhaps surprising in view of the widespread mucus plugging of the small airways that has been reported in asthma. The absence of a significant veno-arterial shunt could perhaps be explained on the basis of a diversion of blood flow from non-ventilated areas of the lungs as a result of pulmonary vasoconstriction.

A large number of studies on regional pulmonary ventilation and perfusion in asthmatics using lung scanning following the inhalation of radioactive gases such as Xe^{133}, the intravenous injection of I^{131} macroaggregated albumin, as well as the inhalation of an aerosol containing Tc^{99m} — iron complex, have now been carried out both during the acute attack and in remission (Woolcock et al 1966; Mishkin & Wagner 1967; Mishkin et al 1968; Hechscher et al 1968; Wilson et al 1970; Despas et al 1970). Most measurements showed well demarcated local ventilation and perfusion defects. Although the areas of hypoventilation generally showed decreased perfusion, it has been reported (Wilson et al 1970) that the perfusion was frequently less effected than ventilation. Lung scans showed that the V/Q imbalance frequently appears to be widespread in asthma. In general, repeated studies during improvement of symptoms showed normalisation of ventilation-perfusion patterns in areas which were previously involved; however, defects arising in new areas have also been observed (Mishkin et al 1968; Heckscher et al 1968).

Novey and his associates (1970) have studied early ventilation-perfusion changes following the induction of asthma by means of pollen, metacholine and exercise. They reported multiple focal V/Q abnormalities appearing within minutes of induction of asthma. The regional ventilatory abnormalities were greater than those of perfusion although similar in distribution. Although hypoxia is generally accepted as being mainly responsible for local pulmonary vasoconstriction, other mechanisms may also be involved in the causation of regional blood flow defects. These include mechanical occlusion of the capillaries by high intra-alveolar pressure at sites of regional hyperinflation. (Despas et al 1970).

Conclusion

Although no agreement has yet been reached on a definition of asthma (Working Group on the Definition of Asthma 1971), none would contest that the main pathophysiological hallmark of this disease is a variable increase in airway resistance to the flow air due to widespread narrowing of the airways. The actual site of such narrowing is still a matter of some controversy. Evidence for obstruction at both a peripheral level (Cade et al, 1971; Chan-Yeung; 1973) as well as in the large airways (Dulfano, 1966; Mildon et al, 1974) has been produced. It is probable that narrowing is present in both the large as well as in the small airways (Ellul-Micallef, 1974); small airways narrowing being the determining feature in acute asthma. Hyperinflation frequently occurs and it has now become widely recognized that this may be present when the more common spirometric indices used for detecting airway narrowing are normal; indicating an attempt on the part of the asthmatic patient to overcome the obstruction present by breathing at a higher lung volume. Further research is necessary to elucidate the precise nature of the changes in lung elastic recoil and pulmonary diffusing capacity that have been reported in asthma. Blood gas changes in the disease, often of a severe nature, are now an established fact and appear to be mainly due to V/Q abnormalities.

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