CONCLUSIONS

A number of aspects of body plethysmography were investigated in this study: measurement of airway resistance and thoracic gas volume, the relationship of these variables with other parameters of lung mechanics, with indices of alveolar ventilation and with arterial blood gases. Furthermore the influence of a bronchodilating drug (thiazinamium, Multergan®) was assessed in patients with chronic obstructive lung disease. We will summarize the results of this study in the order in which they were presented in the previous chapters.

9.1 THORACIC GAS VOLUME

The plethysmographic measurements of thoracic gas volume during quiet breathing in healthy subjects agree well with those obtained with the closed system helium dilution method, indicating that in these subjects gas trapping does not occur. Consequently in healthy subjects the plethysmographic method does not provide information on lung volume which cannot be obtained with the gas dilution method which is cheaper. Even so an apparent advantage of the body plethysmograph is that many replicate determinations of thoracic gas volume can be made in the time needed to measure the functional residual capacity only once.

Many investigators measure the thoracic gas volume on panting subjects, i.e. immediately after a satisfactory flow-box pressure tracing is obtained during panting, the shutter in the mouthpiece is activated and a mouth pressure-box pressure tracing recorded. We have found that panting is performed at a little larger lung volume than quiet breathing. This implies that when one compares normal values of the functional residual capacity with the observed values of thoracic gas volume, it is better to make measurements at the end of a quiet expiration. Alternatively it is necessary to establish new normal values for the plethysmographic measurements.

In patients with chronic obstructive lung disease the lung volume measured with the plethysmograph is almost invariably larger than the one assessed with the closed system helium dilution method. The discrepancies are larger the severer the airway obstruction. The gas dilution
method provides information on the volume of the ventilated lung spaces, i.e. the volume available for gas exchange. Clearly this information differs from the one obtained with the body plethysmograph, because the last one includes a variable lung volume which is not accessible during normal breathing. Here the plethysmograph provides additional information on the patient. This can be used in a number of ways. In the presence of airway obstruction the volume of trapped gas indicates to what extent lung volumes are underestimated by the gas dilution method, providing a measure of functional disorder of its own right. In the absence of airway obstruction the difference between thoracic gas volume and functional residual capacity indicates e.g. the content of a lung cyst or the volume of gas in a pneumothorax. The combined use of the plethysmographic and gas dilution method is also useful in studies on the effects of a bronchodilating drug. Because the functional residual capacity, the pulmonary nitrogen emptying rate and the slope of the alveolar plateau of the nitrogen wash-in curve were not significantly altered by thiazinamium, one might conclude that this drug affected neither the lung volume nor the distribution and efficiency of ventilation. The results presented in chapter 5, however, indicate that both the resting expiratory lung volume and the volume of trapped gas were significantly reduced after administration of the bronchodilator. Consequently the slope of the nitrogen multiple single breath curve and the pulmonary nitrogen emptying rate do not refer to the same lung volume, even though their absolute values before and after bronchodilation remained unchanged.

Plethysmographic measurements of lung volume in patients can be replaced to some extent by modifications of the gas dilution method. The modification proposed by Reichel (1968) — repeated vital capacity manoeuvres and control of the oxygen concentration in the spirometer during the measurements — or the helium rebreathing method developed by Visser and Kowalski (to be published) provide information which is equivalent to the one obtained with the plethysmograph. This is only true as long as airways open up during a vital capacity manoeuvre. In the presence of gas spaces which do not communicate with the airways, or airway occlusion e.g. caused by tumors, the plethysmograph will yield the higher lung volumes. Prolongation of mixing or rinsing times is not an attractive solution for the patient and introduces an error in the measurement due to diffusion of the tracer gas into or out of the blood and tissues.

9.2 AIRWAY RESISTANCE

The panting method is an elegant solution for a number of technical problems associated with the measurement of alveolar pressure. It was our experience that very obstructed patients found it very difficult to
limit their tidal excursions at panting frequency. In these subjects the measurements took a rather long time. Furthermore expiratory looping was less frequently observed during panting than during quiet breathing. This looping was peculiar to patients with airway obstruction, providing important qualitative information on the subject's condition.

The rebreathing method was not very well suited for the quick assessment of airway resistance. The dissipation of heat from the bag, and the occurrence of hyperventilation due to accumulation of carbon dioxide made the prolonged stay in the plethysmograph rather unpleasant. In this connection it should be mentioned that airconditioning of the interior of the plethysmograph contributed greatly to subject comfort. For this reason we recommend its application strongly, especially if the instrument is used in clinical investigations.

The subtraction method combined ease of operation with rapid assessment of airway resistance during quiet breathing. This method did not inconvenience the patient in any way. A disadvantage of this method was that measurements were a little more difficult in normal subjects than with the panting method. In paragraph 9.5 we will pay attention to the problem of correct simulation of BTPS conditions with the subtraction method.

The comparison of the three methods for measuring airway resistance showed insignificant differences in healthy subjects between the panting and rebreathing method. The subtraction method indicated airway resistance a little lower than the two other methods for reasons which are obscure. In patients with chronic obstructive lung disease the two quiet breathing methods yielded equivalent results with respect to the value of airway resistance and the shape of the resistance curve. The panting method indicated airway resistance a little lower; although the difference was statistically significant, it was negligible for practical purposes.

After administration of thiazinamium airway resistance was significantly reduced (40 per cent) in patients with obstructive lung disease, regardless of which method was used. The shape of the flow-box pressure tracing was also influenced in that expiratory looping occurred less frequently. This might be due to a decrease in the volume of trapped gas, less widespread closing of airways during the respiratory cycle, and to a significant decrease in the time-constants of lung units (which would decrease the phase difference between pressure and flow).

9.3 AIRWAY RESISTANCE, VISCous WORK OF BREATHING AND ONE-SECOND FORCED EXPIRATORY VOLUME

The plethysmographic measurements of airway resistance are more sensitive to pathology of the larger airways than of small airways. The reverse applies to the forced expiration method. In chapter 7 we have
explained that a forced expiration leads to dynamic compression of the larger airways. Application of still greater pressures to the lungs causes the resistance of the compressed segments to rise further. In that situation the expiratory flow rate is mainly determined by the resistance of uncompressed airways and elastic lung recoil. Since the dynamics of a forced expiration are usually quite different from those of a quiet breath, the rather good correspondence between airway resistance and one-second forced expiratory volume expresses a complex relationship rather than a simple one. Because of these differences plethysmographic measurements of airway resistance are particularly useful when combined with the determination of the forced expiratory volume. If e.g. the forced expiration method indicates pathology and airway resistance is normal, this may indicate small airway disease, loss of elastic lung recoil, or both. On the other hand severe obstruction of the smaller airways may lead to the development of pressures during a normal expiration sufficient to cause dynamic airway compression, especially if accompanied by loss of elastic lung recoil. Plethysmographic measurements will then reveal a high airway resistance; this information is then not specific for intrinsic obstruction in the larger airways because it reflects in part the effects of dynamic airway compression.

One of the factors that should be taken into account when evaluating the absolute values of airway resistance is the volume at which it is determined. This can be done by using either the product of airway resistance and thoracic gas volume, or more properly the slope of the conductance-volume line. The last method requires many measurements of airway resistance at different lung volumes and cannot be easily applied in patients with obstructive lung disease. Substitution of the product of resistance and lung volume for airway resistance resulted in a significantly better correlation with the one-second forced expiratory volume in subjects with chronic obstructive lung disease with roentgenologic signs of emphysema, but not in obstructed patients without signs of emphysema.

The good correspondence between simultaneously assessed viscous work of breathing and airway resistance in patients with chronic obstructive lung disease without signs of pulmonary fibrosis indicates that one method may replace the other one. Therefore such measurements can be made more conveniently in the body plethysmograph if one does not require information on the elastic properties of the lungs. Flow-box pressure tracings may be used solely, because airway resistance calculated from these curves correlates very well with the one from a volume-box pressure tracing. In addition the shape of flow-box pressure curves provides relevant qualitative information which is not so easily obtained from the volume-box pressure diagram.
The results presented in chapter 8 demonstrate that there was no correlation between the distribution of ventilation and airway resistance. The absence of correlation implies that measurements of airway resistance are useful: information obtained with one method is supplementary to the information obtained with the other method, each one illuminating different aspects of pulmonary function. There was a tendency towards more even ventilation distribution after the administration of thiazinamium. On the other hand there was an indication that the wash-out of the poorly ventilated lung spaces, as judged from the pulmonary nitrogen emptying rate, became somewhat poorer after bronchodilation. This may reflect more extensive closing of airways during part of the respiratory cycle, or an increase in the volume of the poorly ventilated space due to opening up of previously non-ventilated compartments.

It was found that elevations of airway resistance were usually accompanied by insufficient matching between ventilation and perfusion, as judged from the arterial oxygen tension. The correspondence between both variables was not close enough to allow an accurate prediction of the arterial oxygen tension from airway resistance. After bronchodilation with thiazinamium a significant improvement occurred in thoracic gas volume and airway resistance, but neither in ventilation distribution nor in arterial blood gases. The main effect of this bronchodilator was therefore an improvement in lung mechanics. The gain for the patient was a significant reduction in viscous work of breathing. The unaltered arterial oxygen tension after bronchodilation in the presence of a presumably reduced volume of trapped gas may be a result of ventilation in non-perfused lung zones which were previously not ventilated, or to shifts in ventilation and perfusion which preserved the previously existing balance between the two.

The group of subjects in whom this part of the investigation was performed was inhomogeneous. It is desirable that further investigations are carried out in more homogeneous groups. In these groups the effect of a bronchodilating drug can be studied better when other parameters of alveolar ventilation and perfusion are also available. In this context e.g. nitrogen wash-out curves obtained by plotting the logarithm of the end-tidal nitrogen concentration versus the cumulative expired volume, the Becklake index, or the study of the continuous distribution of specific tidal volume (Gómez and Filler, 1966) should be mentioned. These techniques require equipment which was not available during the present study. Another relevant technique is the study of the regional distribution of ventilation and perfusion, using radioactive isotopes.
9.5 COMPLICATING FACTORS

9.5.1 TECHNICAL

Although the use of the subtraction method offers a number of advantages, it has a drawback. The correction of box pressure changes for the effects of the difference in temperature and saturation of inspired and expired gas is established on subjects without cardiorespiratory disease. It is, however, possible that the temperature of gas in the lungs of different subjects varies, and that small changes in the temperature and saturation of gas in the plethysmograph occur. Even though the error thus introduced in measurements of airway resistance is not great in obstructed patients, it would be desirable to have more certainty that these errors do not influence the results. For this reason experiments are now being carried out with a new system which provides gas at BTPS conditions. It consists of a vessel containing water. The temperature of the water is thermostatically controlled by the temperature difference between inspired and expired gas. Air from the plethysmograph is intimately mingled with the water in the vessel by means of a centrifugal pump, and circulated at a flow rate of 1 l sec\(^{-1}\) by means of a ventilator to an insulated dome inside the plethysmograph, from which the subject inhales. This BTPS system and the plethysmograph form a closed system. Because the dome is open the system offers no resistance to airflow; the problem of condensation of water in the polyethylene bag of the BTPS system used in the present investigation is not present any more, eliminating artificial changes in the shape of pressure-flow curves due to gravitational factors. Use of the new BTPS system would lead to a rapid rise in the temperature and saturation of gas inside the plethysmograph, but this is counteracted by airconditioning. It is hoped that this method may in due time replace the subtraction method. Insufficient experience is as yet available to judge its practicability.

9.5.2 BIOLOGICAL

The existence of rhythmic variations in many functions, among them pulmonary function, has been described by numerous authors. The poorest values during the daytime in these pulmonary function parameters are observed early in the morning. Improvement then occurs, reaching a maximum a little after noon, after which some deterioration commences. The investigations performed in patients took 4—4½ hours; the results may therefore have been influenced by naturally occurring changes in the pulmonary function. On the other hand these rhythmic changes have probably not influenced the conclusions since the effects were cancelled out by the fact that the investigations were started in the morning in half of the patients, and in the afternoon in the remaining patients.
Very little is as yet known about the time relationship between the effect of drugs on lung mechanics and on haemodynamics. If phase differences occur between changes in airway resistance, alveolar ventilation and pulmonary perfusion after the administration of a drug, these can only be detected by repeated measurements at constant time intervals. This was not feasible in the present study because the measurements which were performed took already much of the patient's time. Nevertheless studies in which attention is paid to this aspect of drug effects may well shed new light on the properties of different drugs, and on the interrelationships between many parameters of pulmonary function in different types of patients.

9.6 USEFULNESS OF PLETHYSMOGRAPHIC MEASUREMENTS

In the preceding paragraphs and chapters evidence has been presented which demonstrates that plethysmographic measurements of airway resistance and thoracic gas volume provide useful information which cannot be obtained with other methods. Each technique illuminates different aspects of pulmonary function. It is therefore clear that the body plethysmograph should not be used to replace other methods, but rather that the combined use of these methods should be recommended.

Many people believe that the plethysmograph is more sensitive in assessing airway obstruction than the forced expiration method. It is our view that measurements of airway resistance and the forced expiratory volume are not equivalent. We have demonstrated that a normal airway resistance may be found in subjects in whom the one-second forced expiratory volume is abnormal, indicating obstruction in small airways to which plethysmographic measurements are not very sensitive. On the other hand we have frequently been able to perform measurements in the plethysmograph in patients for whom the forced expiration method was too strenuous.

The curvilinear relationship between airway resistance and one-second forced expiratory volume (fig. 7.2 and 7.6) suggests that minor degrees of airway obstruction are more easily detected with a forced expiration method. For this reason we believe that plethysmographic measurements of airway resistance are not very useful in epidemiological studies. These studies deal with a population in which airway obstruction is present in only a minor proportion of the subjects, in the majority of cases not being severe. Because forced expiration methods are much simpler, less expensive and not less sensitive in detecting airway obstruction, we believe that these should be favored. The plethysmograph is, however, very suited for measurements of lung volumes since these can be performed both accurately and rapidly.

The body plethysmograph is an expensive and rather complicated instrument. For this reason it does not belong in every pulmonary
function laboratory. Proper use of the instrument can only be made, in our opinion, in laboratories in which sufficient know-how is present with regard to pulmonary pathophysiology, measurement of flow and pressures, physical and electronic problems. This is usually the case in the larger laboratories, in which also sufficiently trained laboratory personnel is to be found. Here the plethysmograph can be properly used for routine and research purposes. It is our experience that the use of the plethysmograph stimulates the thinking about pulmonary pathophysiology and thus in the long run promotes a better understanding of mechanisms in lung disease. This in itself is sufficient justification for the investment.

REFERENCES