OBESE PEOPLE ARE AT INCREASED risk of respiratory symptoms, such as breathlessness, particularly during exercise, even if they have no obvious respiratory illness (4, 45). Obesity has a clear potential to have a direct effect on respiratory well-being, since it increases oxygen consumption and carbon dioxide production, while at the same time it stiffens the respiratory system and increases the mechanical work needed for breathing. The association between obesity and asthma has also raised new concerns about whether the mechanical effects of obesity on the respiratory system contribute to airway dysfunction that could induce or worsen asthma. This review will explore the effects of obesity [body mass index (BMI) \( \geq 30 \) kg/m\(^2\)] on “normal” pulmonary physiology. The more substantial derangements associated with the obesity-hypoventilation syndrome are the subject of another review in this series.

LUNG VOLUMES

The most consistently reported effect of obesity on lung function is a reduction in the functional residual capacity (FRC) (28, 40). This effect reflects a shift in the balance of inflationary and deflationary pressures on the lung due to the mass load of adipose tissue around the rib cage and abdomen and in the visceral cavity (52). There is an exponential relationship between BMI and FRC (28, 40), with a reduction in FRC detectable even in overweight individuals (28). In obesity, the reduction in FRC may become so marked that the FRC approaches residual volume (RV).

However, the effects of obesity on the extremes of lung volumes, at total lung capacity (TLC) and RV, are modest. Many studies report an association between increasing body weight and decreasing TLC (11, 28, 42); however, the changes are small, and TLC is usually maintained above the lower limit of normal, even in severe obesity (11, 28, 63). The RV is usually well preserved (5, 11, 48, 63, 67), and the RV-to-TLC ratio remains normal or slightly increased (5, 28). In the presence of a modest reduction in TLC and a well-preserved RV, the reduction in FRC is manifested by an increase in inspiratory capacity and a very marked decrease in the expiratory reserve volume (ERV) (28).

The reasons for the reduction in TLC are not known, but it is probably due to a mechanical effect of the adipose tissue, since TLC is increased by weight loss in both mild (64) and morbidly obese (60) subjects. A reduction in the downward movement of the diaphragm, due to increased abdominal mass, is likely to decrease TLC by limiting the room for lung expansion on inflation. Alternatively, deposition of fat in sub-
pleural spaces (49) might directly reduce lung volume by reducing the volume of the chest cavity, although there is no direct evidence of any association between subpleural fat and either body fat or lung volumes. Evidence that respiratory muscle strength and maximum inspiratory and expiratory pressures are similar in obese and normal weight subjects (29, 48, 65) suggests that stiffening of the chest wall is probably not a major determinant of TLC.

**FAT DISTRIBUTION AND BODY COMPOSITION**

BMI is a global measure of body mass that includes both fat and lean mass and takes no account of differences in fat distribution. If the reduction of lung volumes in obesity is due to a direct mechanical effect on lung volumes, then the distribution of body fat should modify the relationship between BMI and lung volumes. Abdominal and thoracic fat are likely to have direct effects on the downward movement of the diaphragm and on chest wall properties, while fat on the hips and thighs would be unlikely to have any direct mechanical effect on the lungs. Both abdominal fat, measured by waist circumference (10), waist-to-hip ratio (7), or abdominal height (37), and thoracic or upper body fat, measured by subscapular skinfold thickness (31) or biceps skinfold thickness (11), are associated with reductions in lung volumes. Several studies have used dual-energy X-ray absorptiometry (DXA) to quantify fat and lean mass in different regions of the body and relate these findings to lung function (12, 58). Sutherland et al. (58) used a wide range of body fat variables to determine the effect of fat distribution on lung volumes in healthy adults. Lung volumes were only loosely associated with BMI, but both DXA and non-DXA-derived variables reflecting upper body fat had highly significant negative correlations with FRC and ERV in both men and women. There were no differences in the strength of these associations between the markers of abdominal obesity (waist circumference, waist-to-hip ratio, DXA waist fat, DXA abdominal fat) or thoracic fat (DXA trunk fat, DXA thoracic fat). These findings confirm the important effect of upper body fat on the lung, but the inability to differentiate the effects of abdominal and thoracic fat suggests that they may be interdependent.

**LUNG AND RESPIRATORY SYSTEM MECHANICS**

Obesity is characterized by a stiffening of the total respiratory system (35), which is presumed to be due to a combination of effects on lung and chest wall compliance (41). Most studies have demonstrated a reduction in lung compliance in obese individuals (21, 40, 41, 53) that appears to be exponentially related to BMI (40). Reductions in lung compliance may be the result of increased pulmonary blood volume, closure of dependent airways, resulting in small areas of atelectasis (21), or increased alveolar surface tension due to the reduction in FRC.

Evidence for an effect of obesity on chest wall compliance varies between studies, possibly as a result of methodological differences. Measurement of chest wall compliance is difficult, since the respiratory muscles must be relaxed and inactive to allow an accurate measurement. Studies of conscious, spontaneously breathing subjects have suggested that there is a reduction in chest wall compliance in obesity (35). However, normal chest wall compliance has been reported in studies of anesthetized, paralyzed subjects in mild (40) or severe (21) obesity, as well as in studies of conscious subjects using different measurement techniques (53, 55). Sharp et al. (52) found that mass loading of the thorax in normal weight conscious or anesthetized/paralyzed subjects produces a parallel rightward shift of the chest wall pressure-volume curve without affecting compliance. The chest wall pressure-volume curve of obese subjects resembled that of normal subjects with mass loading of the thorax. Excess body mass in simple obesity may act as an inspiratory threshold load, and, once the threshold is overcome, the chest wall behaves normally.

**AIRWAY FUNCTION**

Spirometric variables, such as forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), tend to decrease with increasing BMI (51, 54, 67). However, the effect is small, and both FEV₁ and FVC are usually within the normal range in healthy, obese adults (51, 54) and children (50). The FEV₁-FVC ratio is usually well preserved or increased (31, 44, 51, 54, 67), even in morbid obesity (5), indicating that both FEV₁ and FVC are affected to the same extent. This finding implies that the major effect of obesity is on lung volumes, with no direct effect on airway obstruction.

Similarly, expiratory flows decrease with increasing weight (5, 44), in proportion to the lung volumes (67). A decrease in expiratory flows in an obese individual is unlikely to indicate bronchial obstruction, unless the flow measurements have been normalized for the reduction in vital capacity. Figure 1 shows flow volume loops from a healthy obese woman with significant reduction in lung volumes, but very well preserved expiratory flows. However, the expiratory flow at 50% of the reduced vital capacity is low compared with the predicted value, based on the predicted vital capacity. In a large sample of obese and normal weight nonsmokers, Rubenstein et al. (44) found significant reductions in expiratory flows in obese men, but not in obese women. The difference between obese and

![Flow-volume loops from healthy obese female, aged 35 yr, BMI = 43 kg/m², with reduced total lung capacity (TLC), functional residual capacity (FRC), and vital capacity, but well-preserved expiratory flows. The dashed line shows the predicted flow-volume loop, the solid line is the actual loop. The predicted lung volumes are shown on the bar, vertical arrow shows predicted flow at 50% vital capacity, and horizontal arrow shows the actual value. RV, residual volume.](image-url)
normal weight men in expiratory flow at 50% of the reduced vital capacity disappeared after normalization for vital capacity. However, significant differences in expiratory flow at 25% of the reduced vital capacity persisted after normalization, suggesting the possibility of peripheral airway obstruction in obese men.

Mechanical properties of the airway, such as resistance and reactance, are highly dependent on lung volume and are, therefore, affected by any reduction in FRC. Respiratory resistance is increased in the obese (65), indicating that airway caliber is reduced throughout the tidal breathing cycle. However, specific airway resistance, calculated by adjusting for the lung volume at which the measurements were made, is in the normal range (36, 44, 65, 67), so that the apparent reduction in airway caliber in the obese is attributable to the reduction in lung volumes rather than to airway obstruction. However, some studies have suggested that the increase in resistance may not be due entirely to the reduced lung volume, since differences between obese and nonobese may persist after adjustment for lung volumes (30, 63). The cause of the additional resistance is unknown, and it is unclear whether there are any structural changes in the airways of the obese. It is possible that airway structures could be remodeled by exposure to proinflammatory adipokines, or damaged by the continual opening and closing of small airways throughout the breathing cycle (34). It is not known whether fat is present in the airways of obese people or has any direct effect on airway structure, but studies of diet-induced obesity in rats have reported changes in lipid deposition in the lungs (26), which may affect surfactant function (25). There is some evidence that peripheral airway obstruction may be increased in the obese, since the frequency dependence of resistance increases with increasing obesity (67). Furthermore, frequency dependence of compliance was increased in a group of morbidly obese subjects who had normal lung compliance, but very low ERV (16). Longitudinal studies of the effects of weight loss might be enlightening, since improvements in lung volumes after weight loss that are not accompanied by improvements in volume-adjusted airway caliber could suggest that there is a persistent remodeling of the airways, rather than a direct mechanical effect on airway caliber.

Breathing at low lung volume places the tidal flow volume loop in a region where it may encroach on the maximal flow volume envelope (Fig. 1) and thus increase the risk of expiratory flow limitation in the obese individual. However, it is not clear whether expiratory flow limitation is a common occurrence in the obese. Two studies (18, 39), using the negative expiratory pressure technique, have found that expiratory flow limitation only occurred in ~20% of severely obese subjects when upright, but both expiratory flow limitation and breathlessness increase substantially when the subjects are supine. However, the negative expiratory pressure technique uses a forced expiration and may not be able to detect expiratory flow limitation that occurs during tidal breathing at low lung volumes. Ofr et al. (38) quantified expiratory flow limitation from the flow-volume loop, as the percentage of the tidal volume that encroached on the maximal flow envelope, and found highly significant differences between obese and normal weight women seated at rest. New techniques are available for measuring expiratory flow limitation during tidal breathing, based on the forced oscillation technique (13), that would allow larger studies to determine the extent of expiratory flow limitation in obese populations.

TIDAL VOLUMES

Tidal volumes are often reduced in severe obesity, and breathing follows a rapid, shallow pattern (48). This pattern is likely to be a response to the increased stiffness of the respiratory system, since a rapid, shallow breathing pattern is a typical response to an elastic load (1), which can be induced in normal weight subjects with elastic strapping of the chest (8). During exercise, obese subjects preferentially increase their breathing frequency more, and tidal volumes less, than nonobese subjects (15, 38). Similar changes occur during bronchoconstriction in association with increasing elastic loads, represented by increasing respiratory system elastance (47). However, in mild-moderate obesity, tidal volumes at rest are often in the normal range (6, 38, 47, 62), and the frequency and magnitude of regular sighs and deep inspirations appear similar to those in normal weight subjects (6, 62). This suggests that the modulation of airway smooth muscle contractility by regular tidal stretching and deep inspirations (19) may be unimpaired in mild-moderate obesity.

AIRWAY CLOSURE, VENTILATION DISTRIBUTION, AND GAS EXCHANGE

As FRC is reduced to the extent that it approaches RV, the obese individual is at increased risk of airway closure and abnormalities of ventilation distribution. Indicators of gas trapping and airway closure, such as RV (48, 63) and closing capacity (22), are not usually increased in the obese at rest. However, there is consistent evidence that, because the FRC is so low, closing capacity exceeds the FRC, and airway closure can occur within the tidal breaths (17, 20, 22, 34). Closing capacity, and particularly the extent to which closure occurs within the range of tidal breathing, has been correlated with arterial PO2 (17, 22), raising the possibility that airway closure during tidal breathing is associated with underventilation of some regions of the lung.

Physiological studies using single breath or multibreat washout tests suggest that heterogeneity of ventilation is normal or close to normal, even in extreme obesity. Heterogeneity of ventilation distribution, measured by slope of phase III from single-breath washouts or by lung clearance index, is normal in the obese (22). However, studies using imaging techniques reveal abnormalities of regional ventilation in some obese individuals. In an upright nonobese individual, the distribution of regional ventilation is greatest in the lower, dependent lung zones and decreases toward the upper zones. In obese individuals, this distribution may be reversed (14, 23, 24). Holley et al. (23) found that, in obese subjects with marked reductions in ERV to ~20% predicted, ventilation was preferentially distributed to the upper zones of the lung, leaving the lower, dependent zones relatively underventilated. Demedts (14) found reduced regional ventilation in the lower zones in obese subjects, consistent with relative air trapping in the bases. While the mechanism for this underventilation and air trapping in the bases is not clear, Demedts suggests that it is unlikely, due to intrinsic changes in the airways that cause them to close at higher transpulmonary pressure. Instead, he suggests that limitations in chest wall and diaphragm movements alter the
configuration of the lungs and enhance basal air trapping at low lung volumes. The distribution of perfusion is predominantly to the lower zones, so those obese individuals with a reversal of the normal distribution of ventilation are at risk of regional ventilation-perfusion mismatch in the dependent zones of the lung (23).

Mild hypoxemia and increased alveolar-arterial oxygen difference are frequently reported, even in eucapnic obese individuals (21, 22, 27, 40, 60), and have been associated with abdominal obesity in the morbidly obese (66). However, the effect of weight loss on gas exchange is variable, since some studies show improvements in arterial oxygen tensions (43, 60), while others report no change (20, 64), despite a concurrent reduction in closing capacity (20). Most studies suggest that lung CO-diffusing capacity is normal (15, 42, 53, 57), even in morbid obesity (5). However, some studies suggest it may be increased in extremely obese subjects (42, 44), probably as a result of the increase in blood volume (42).

BREATHELESSNESS DURING EXERCISE AND AT REST

Breathlessness during exercise is a common complaint among obese individuals, but the mechanisms that drive these symptoms are not well defined. In severely obese subjects, Dempsey et al. (15) found that, even during maximal exercise on a cycle ergometer, these subjects were able to increase their ventilation sufficiently to avoid hypercapnia. Furthermore, the ventilatory response to inhaled CO₂ in these obese subjects was not different from that in a normal weight control group (15). Peak exercise capacity, in terms of both peak work rate and oxygen consumption, is normal in healthy obese subjects (2, 3, 38). Ofir et al. (38) compared obese and normal weight women during cycle exercise and found that, although oxygen consumption and minute ventilation were greater in the obese subjects at all work rates, the relationships between breathlessness scores and both oxygen consumption and minute ventilation were no different in the obese and normal weight subjects. The implication of this finding is that the determinants of breathlessness were similar in obese and normal weight subjects, and that respiratory mechanical factors related to obesity did not contribute to breathlessness in the obese subjects. Babb et al. (3) found there was no difference in peak exercise capacity between obese women with and without exertional breathlessness; however, breathlessness was associated with a greater increase in the oxygen cost of breathing during exercise.

Breathlessness at rest may also be reported by obese individuals (4, 45), but it is unclear if this is due entirely to obesity. Sahebjami and Gartsdie (45, 46) found that, among 23 healthy obese men, the 15 who reported breathing difficulties at rest had lower maximum voluntary ventilation and lower maximal expiratory flows at low lung volumes. The dyspneic group also included a greater proportion of smokers, which may account for some of the symptoms and differences in lung function. However, the link between breathlessness and poor performance on a test of maximum voluntary ventilation may be associated with an increase in the oxygen cost of breathing, since the oxygen cost of breathing increases parabolically with breathing frequency (33).

EFFECTS OF BRONCHOCONSTRICTION ON LUNG FUNCTION IN THE OBESE

Recent interest in the association between obesity and asthma raises the question of whether the physiological effects of obesity modulate the pathophysiology of asthma. Nicola-cakis et al. (36) suggest that obesity and asthma have additive, rather than synergistic effects, on outcomes such as spirometry and lung volumes, implying that asthma and obesity affect the respiratory system through different processes. It remains unclear whether there is any association between obesity and airway hyperresponsiveness, a characteristic feature of the pathophysiology of asthma. However, the reduction in operating lung volume in the obese has the potential to modify the effects of bronchoconstriction and increase the occurrence of expiratory flow limitation. Bronchoconstriction in the obese is associated with increased airway closure compared with nonobese controls (9) and thus could increase gas trapping and alter ventilation distribution, but there are no published data about the effect of bronchoconstriction on ventilation distribution in the obese. Bronchoconstriction causes greater hyperinflation in obese asthmatic (56) and nonasthmatic (47) subjects, which may increase the severity of dyspnea (32). The occurrence of additional elastic loads during bronchoconstriction, reflected by greater changes in respiratory system reactance in obese than nonobese subjects (47, 62), which are not well reflected by spirometry, may explain why some obese asthmatic subjects have more severe symptoms than their lean counterparts, despite similar spirometry (61). In patients with moderate chronic obstructive pulmonary disease, a simulated increase in body weight of 10 kg resulted in a marked reduction in exercise performance (59), suggesting that the combination of increased weight and airway obstruction could have a substantial effect on respiratory well-being.

IMPLICATIONS FOR FUTURE RESEARCH

Although the physiology of obesity and its effects on lung function have been the subject of intense investigation over the last 50 years, the recent observation of the association between asthma and obesity has raised new questions about the mechanical effects of obesity on the lungs, and the mechanisms that drive breathlessness in the obese are still not well understood.

It is still unknown whether obesity has any effect on the structure of the airways, either by altered lipid deposition or by remodeling. Although these questions may be best answered by direct studies of airway pathology, physiological studies of the effects of weight loss on volume-adjusted flow and resistance would also be useful.

Expiratory flow limitation is a potentially important determinant of breathlessness in the obese, although studies using negative expiratory pressure suggest that flow limitation is not a common feature of obesity. However, the negative expiratory pressure technique may be an inappropriate method to detect flow limitation during tidal breathing at low FRC in the obese. Studies using a measurement based on tidal breathing (13) would be useful to determine the prevalence of flow limitation in obese populations and its relationship to lung volume and to breathlessness.

Bronchoconstriction has the potential to enhance some of the effects of obesity, such as airway closure, which may then
affect ventilation distribution. A better understanding of the extent to which obesity modifies the physiological effects of bronchoconstriction may improve our understanding of the relationship between asthma and obesity.

REFERENCES


