

REVIEW

Physiological changes in respiratory function associated with ageing

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ABSTRACT: Physiological ageing of the lung is associated with dilatation of alveoli, enlargement of airspaces, decrease in exchange surface area and loss of supporting tissue for peripheral airways ("senile emphysema"), changes resulting in decreased static elastic recoil of the lung and increased residual volume and functional residual capacity. Compliance of the chest wall diminishes, thereby increasing work of breathing when compared with younger subjects. Respiratory muscle strength also decreases with ageing, and is strongly correlated with nutritional status and cardiac index. Expiratory flow rates decrease with a characteristic alteration in the flow–volume curve suggesting small airway disease. The ventilation–perfusion ratio (V_A/Q') heterogeneity increases, with low V_A/Q' zones appearing as a result of premature closing of dependent airways. Carbon monoxide transfer decreases with age, reflecting mainly a loss of surface area. In spite of these changes, the respiratory system remains capable of maintaining adequate gas exchange at rest and during exertion during the entire lifespan, with only a slight decrease in arterial oxygen tension, and no significant change in arterial carbon dioxide tension. Ageing tends to diminish the reserve of the respiratory system in cases of acute disease. Decreased sensitivity of respiratory centres to hypoxia or hypercapnia results in a diminished ventilatory response in cases of heart failure, infection or aggravated airway obstruction. Furthermore, decreased perception bronchoconstriction and diminished physical activity may result in lesser awareness of the disease and delayed diagnosis.

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During the first two decades of life, the lungs undergo a phase of growth and maturation. The maximal number of alveoli is reached at about 10–12 yrs of age and, thereafter, maturation of the respiratory system accelerates until maximal function is reached, at approximately the age of 20 yrs for females and 25 yrs for males. Throughout the remainder of life, ageing is associated with a progressive decrease in lung performance; however, unless affected by disease, the respiratory system remains capable of maintaining adequate gas exchange during the entire lifespan [1, 2].

The most important physiological changes associated with ageing are: a decrease in the static elastic recoil of the lung, a decrease in compliance of the chest wall, and a decrease in the strength of respiratory muscles. Most of the age-related functional changes described are related to these three phenomena. Also noteworthy are the decrease in the respiratory response to hypoxia and hypercapnia and a diminished awareness of increased airway resistance or elastance. The present review explores the age-related structural changes of the respiratory system and their consequences on respiratory mechanics and gas exchange.

Structural changes in the respiratory system related to ageing

The elastic properties of the lung can be separated into two components: surface forces and tissue forces. There is no evidence to date that the surface-active lining of terminal respiratory units alters its basic mechanical behaviour with age: no change in the quality or quantity of surfactant has been described, nor is there any evidence of changes in type II pneumocyte or Clara cell number or function. However, changes in lung parenchyma and chest wall are functionally significant.

Age-associated changes in the chest wall

Chest wall compliance decreases progressively with age. The stiffening is presumably related to calcification and other structural changes within the rib cage and its articulations, *i.e.* calcification of costal cartilage and rib-vertebral articulations and narrowing of intervertebral disk spaces [1, 3]. Changes in the shape of the thorax also occur as a result of age-related osteoporosis resulting in partial (wedge) or complete (crush) vertebral fractures, leading to increased dorsal kyphosis and anteroposterior (AP) diameter ("barrel chest"). The reported prevalence of vertebral crush fractures in the UK is 2.5% for females aged 60 yrs and reaches 7.5% for those aged 80 yrs. Partial vertebral fractures are found in 60% of females aged ≥ 75 yrs [4]. Males also show an increase in vertebral fractures with age, but rates are approximately half those of females [4]. In a study of 100 chest radiographs of normal subjects aged 75–93 yrs, 25% had severe kyphosis as a consequence of vertebral wedge or crush fractures ($>50^\circ$), 43% had moderate kyphosis ($35\text{--}50^\circ$) and 23% had a normal curvature of the spine [5]. These modifications of the chest wall not only alter its compliance but also modify the curvature of the diaphragm, with a negative effect on its force-generating capabilities.

Changes in respiratory muscle function

Respiratory muscle performance is impaired by the age-related increase in functional residual capacity (FRC) (fig. 1), the decrease in chest-wall compliance and the geometric changes in the rib cage. Both the kyphotic curvature of the spine and the AP diameter of the chest increase with ageing, thereby decreasing the force-generating capacity of the diaphragm [5]. Furthermore, POLKEY *et al.* [7] have shown a significant decrease in the strength of the diaphragm of elderly subjects (mean age 73, range 67–81 yrs) compared with a younger control group (mean age 29, range 21–40 yrs): -13% for transdiaphragmatic pressure (P_{di}) during a maximal sniff and -23% during cervical magnetic stimulation. TOLEP *et al.* [8] also reported values of P_{di} of fit elderly subjects (aged 65–75 yrs) which were 25% lower than values obtained in young adults (aged 19–28 yrs).

Respiratory muscle strength is related to nutritional status, which is often deficient in the elderly. ENRIGHT *et al.* [9] showed significant correlations between maximal inspiratory (MIP) or expiratory (MEP) pressures and lean body mass (measured by bioelectrical reactance) or body weight. ARORA and ROCHESTER [10] showed the deleterious impact of undernourishment on respiratory muscle strength or maximal voluntary ventilation (MVV): the decrease in respiratory muscle strength and MVV was highly signi-

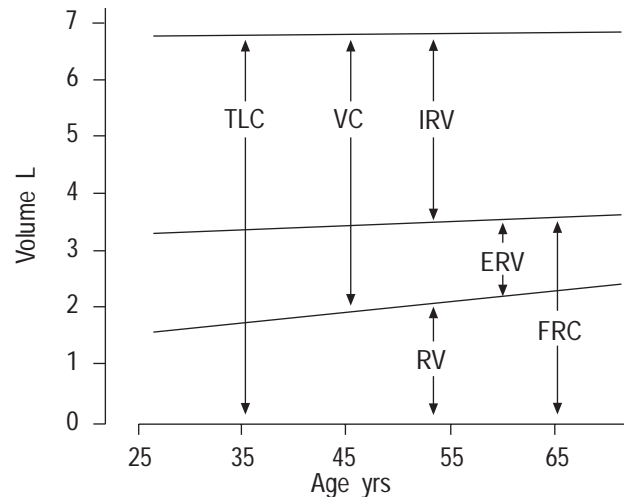


Fig. 1. – Evolution of lung volumes with ageing. TLC: total lung capacity; VC: vital capacity; IRV: inspiratory reserve volume; ERV: expiratory reserve volume; FRC: functional residual capacity; RV: residual volume. (Adapted from CRAPO *et al.*, 1982 [6].)

ficant in undernourished subjects ($71 \pm 6\%$ of ideal body weight (IBW)) compared with control subjects ($104 \pm 10\%$ of IBW). Necropsy studies have confirmed the correlation between body weight and diaphragm muscle mass [11].

Age-associated alterations in skeletal muscles most probably affect respiratory skeletal muscle function [12]. Peripheral muscle strength declines with ageing: a 2% annual decrease in handgrip strength was described in 620 healthy subjects aged >65 yrs by BASSEY and HARRIES [13]. Furthermore, MIP and MEP in elderly subjects are strongly and independently correlated with peripheral muscle strength (handgrip) [9]. Major determinants of the age-related decrease in muscle strength and peak tetanic tension are: a decrease in muscle mass (cross-sectional fibre area); a decrease in the number of muscle fibres, especially type II "fast twitch" fibres and motor units; alterations in neuromuscular junctions; and loss of peripheral motor neurons with selective denervation of type II muscle fibres [12, 14]. Data obtained from adult and aged rats suggest that impairment of the sarcoplasmic reticulum Ca^{2+} pump, owing to uncoupling of adenosine triphosphate (ATP) hydrolysis from Ca^{2+} transport, may contribute to a slowing of contraction (reduced maximal shortening velocity) and relaxation [15]. Decreased synthesis of muscle myosin heavy-chain (*i.e.* decreased "repair" ability) [16] and a decline in mitochondrial respiratory chain function may also contribute to reduced skeletal muscle performance [17–19].

Respiratory muscle function is dependent on energy availability (*i.e.* blood flow, oxygen content, and carbohydrate or lipid levels) [20]. Decreased respiratory muscle strength has been described in patients with chronic heart failure (CHF): EVANS *et al.* [21] showed a significant correlation between cardiac index (CI) and sniff P_{di} , with a proportional reduction in limb muscle strength. NISHIMURA *et al.* [22] made a similar observation in subjects with CHF, showing significant correlations between MIP and CI or maximal oxygen consumption ($V'O_{2,max}$)/body weight (as an index of cardiovascular performance). MANCINI *et al.* [23] showed that CHF has a highly significant impact on

respiratory muscle strength and on the tension–time index (TTI, $P_{di}/P_{di,max} \times t/t_{tot}$) where $P_{di,max}$ is the maximal transdiaphragmatic pressure, t is inspiratory time and t_{tot} is duration of total breathing cycle. The TTI describes the relationship between force of contraction and duration of contraction and is inversely related to respiratory muscle endurance. In elderly subjects with heart failure, the TTI increases, primarily because of an increase in $P_{di}/P_{di,max}$, and, during exercise, approaches values shown to generate fatigue [24].

Other frequent clinical situations decreasing respiratory muscle function in the elderly include Parkinson's disease [25] and sequelae of cerebral vascular disease [26].

Age-associated changes in the lung parenchyma

Static elastic recoil pressure of the lung decreases as a part of normal ageing ($0.1\text{--}0.2\text{ cmH}_2\text{O}\cdot\text{yr}^{-1}$) (fig. 2), these changes are most evident at high lung volumes [27, 28]. With ageing, the static pressure–volume curve for the lung is shifted to the left and has a steeper slope (fig. 3). Explanations are usually attributed to changes in the lung connective tissue. Biochemical studies suggest, however, that the total lung content of collagen and elastin does not change with ageing [30]. Collagen becomes more stable because of increased numbers of intermolecular crosslinks. The present hypothesis is that elastic recoil is lost because of changes in the spatial arrangement and/or crosslinking of the elastic fibre network or because of the presence of a pseudoelastin [3].

Morphometric studies of senescence-accelerated mice (SAM mice; a murine model of accelerated senescence) have shown notable enlargement of alveolar duct size with ageing; the enlargement seen in SAM mice was characterized as relatively homogeneous, without evident destruction. Cellular infiltrates in the alveoli were rarely seen, suggesting that the airspace enlargement did not result from inflammation, as opposed to what is seen in emphysema. Age-related changes in the pressure–volume curves showed a shift leftwards and upwards, *i.e.* loss of elastic recoil of the lung, as described in humans by TURNER *et al.* [27] in subjects aged 20–60 yrs (fig. 3). The ratio of lung

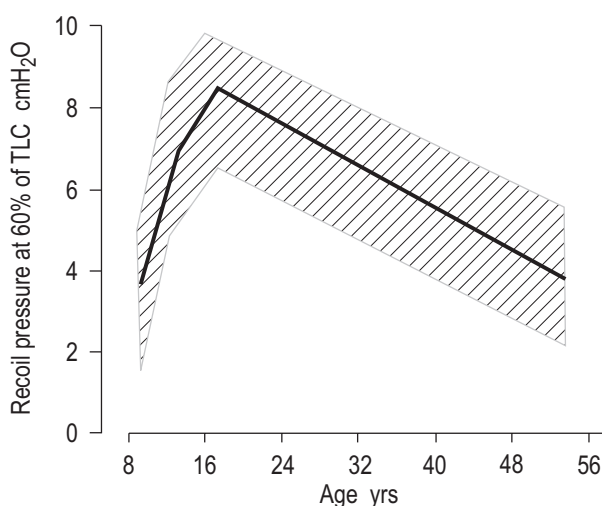


Fig. 2. – Static elastic recoil as a function of age. Static elastic recoil was measured at 60% of total lung capacity (TLC). Shaded area shows ± 1 SD of plotted means. (Adapted from TURNER *et al.*, 1968 [27].)

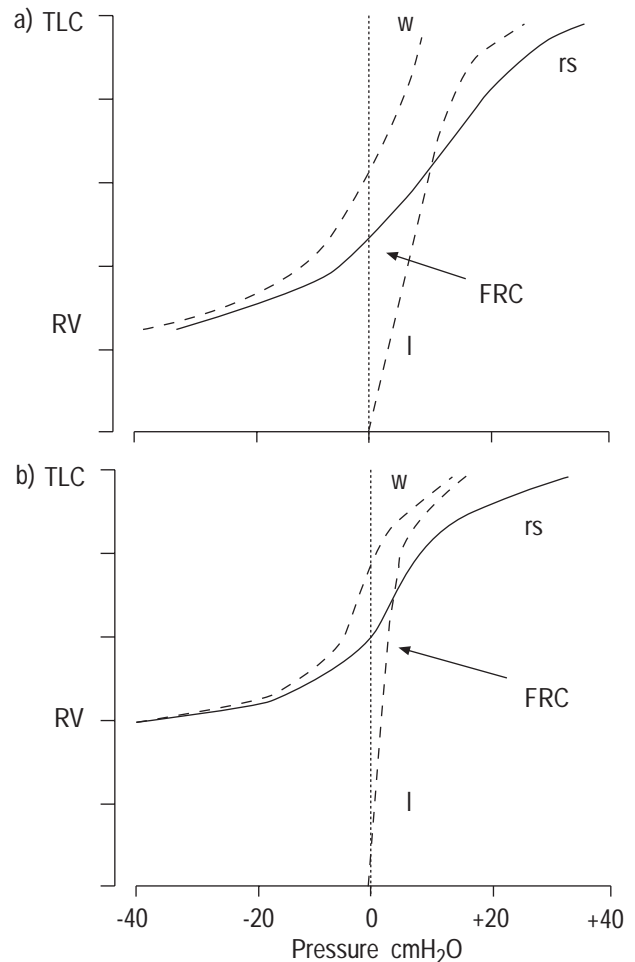


Fig. 3. – Static pressure–volume curve of the lung (l), chest wall (w) and respiratory system (rs) in a) a 20-yr-old and b) a 60-yr-old adult. RV: residual volume; FRC: functional residual capacity; TLC: total lung capacity. (Adapted from TURNER *et al.*, 1968 [28] and MITTMAN *et al.*, 1965 [29].)

weight to body weight did not decrease with ageing, which suggests little or no lung destruction [31]. These changes are similar to those described for senile hyperinflation of the lung in humans. Data suggest that elastic fibres of the lung in SAM mice have a reduced recoil pressure. This results in distention of the alveolar spaces and increased lung volume [32].

As noted in SAM mice during the course of ageing, alveolar ducts in humans increase in diameter and alveoli become wider and shallower (fig. 4a and b). After the age of 50 yrs, a proportion of the elastic fibres in the region of the respiratory bronchiole and alveolus degenerate and appear ruptured and coiled (fig. 5a and b) [33]. These changes are most marked around the alveolar ducts. As a consequence, dilatation of the alveolar ducts occurs and this is followed by enlargement of the airspaces [5]. This enlargement is remarkably homogeneous, as opposed to the irregular distribution of airspace enlargement in emphysema. Morphometric studies have consistently found an increase in the average distance between airspace walls (mean linear intercept (L_m)) and a decrease in the surface area of airspace wall per unit of lung volume (S/V) beginning in the third decade of life. The decrease in S/V is

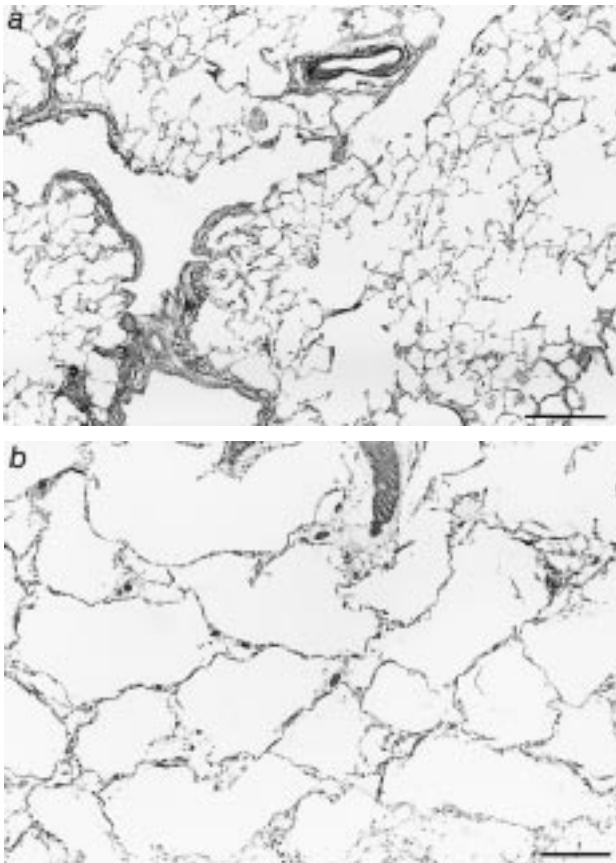


Fig. 4. – Lung parenchyma from a) a nonsmoking 29-yr-old subject and b) a 100-yr-old nonsmoking patient who died from pneumonia. Note marked enlargement of alveoli without any inflammatory infiltrate. (Haematoxylin and eosin stain; internal scale bar=280 μm (a); 250 μm (b).)

approximately linear and continues throughout life, resulting in a 25–30% decrease in nonagenarians [34, 35]. Although these changes are histologically different from emphysema (no destruction of alveolar walls), they result in similar changes in lung compliance. These changes have been designated as "senile emphysema" [33]. A consequence of the reduction in supporting tissues around the airways is a tendency for the small airways (<2 mm) to collapse. Premature closure of the airways may, therefore, occur during tidal breathing. Furthermore, the flattening of the internal surface of the alveoli is associated with a reduction in alveolar surface (75 m^2 at age 30 yrs and 60 m^2 at age 70 yrs, a reduction of $0.27 \text{ m}^2 \cdot \text{yr}^{-1}$) (fig. 4a and b) [3].

The diameter of bronchioles reaches a peak in the fourth decade and declines thereafter. The declining small airway diameter may also contribute to the decrement in expiratory flow with ageing [36].

Pulmonary function tests

Lung volumes

With increasing age, as mentioned previously, the chest wall becomes stiffer, *i.e.* less compliant, but the lungs become more distensible (diminished elastic recoil). As a result, residual volume (RV) increases (air trapping) by approximately 50% between 20 and 70 yrs of age and, during the same period, vital capacity (VC) decreases to about 75% of best values (fig. 1). Increased elastic recoil of

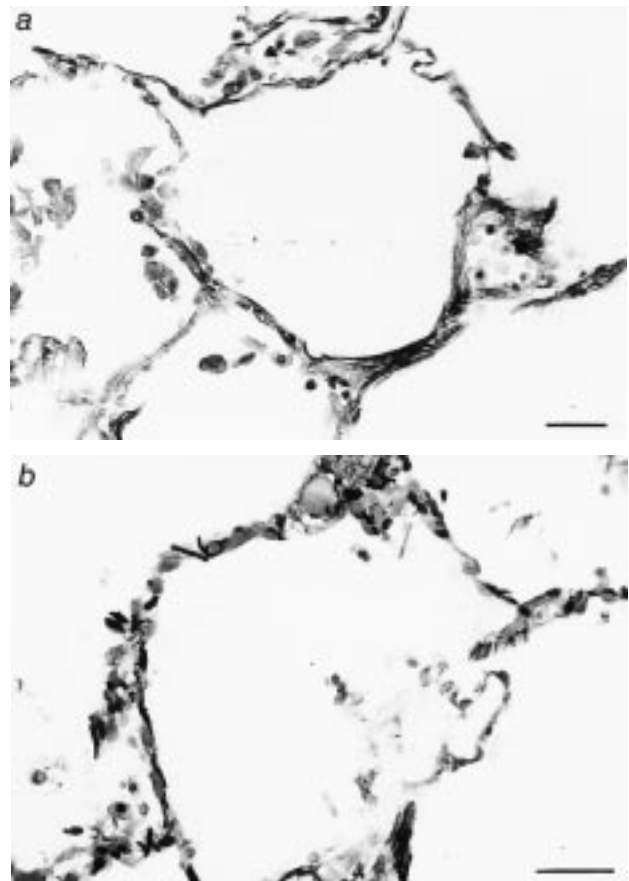


Fig. 5. – Detail of alveolar wall in a) a 29-yr-old subject, showing fine elongated elastic fibres in the alveolar walls and in b) a 100-yr-old subject, showing fragmented rarefied elastic fibres in septae. (Elastin stain; internal scale bar = 35 μm (a); 45 μm (b).)

the chest wall and diminished elastic recoil of the lung parenchyma (fig. 2) also explain the increase in FRC, *i.e.* elderly subjects breathe at higher lung volumes than younger subjects. Because of the shape of the static pressure–volume curve of the respiratory system (fig. 3), the increase in FRC is associated with an increased elastic load from the chest wall, placing an additional burden on the respiratory muscles. During normal resting tidal breathing, the increase in breathing-related energy expenditure in a 60-yr-old male is estimated at 20% compared with that of a 20-yr-old subject.

The closing volume (CV), *i.e.* the volume at which small airways in dependent regions of the lung begin to close during expiration, increases with age. Premature closure of terminal airways is related to a loss of supporting tissues around the airways. CV may reach 55–60% of total lung capacity (TLC), and equal FRC; as such, normal tidal breathing may occur with a significant proportion of peripheral airways not contributing to gas exchange (low ventilation–perfusion ratio ($V'/A/Q'$) zones). This is the major reason for diminished arterial oxygen tension (P_{a,O_2}), increase in alveolar–arterial difference for oxygen, and diminished carbon monoxide transfer with age.

TLC does not change significantly throughout life. The age-related diminished elastic recoil of the lungs is counterbalanced by an increased elastic load from the chest wall.

Spirometry

Forced expiratory volume in one second (FEV₁) and forced vital capacity (FVC) increase up to ~20 yrs of age in females and 27 yrs of age in males, then diminish with advancing age (fig. 6) [37]. Cross-sectional and longitudinal studies both show an accelerated decline in FEV₁ and FVC with age, with the rate of loss being greater in males than in females and more rapid in patients with increased airway reactivity [3]. The annual decrease in FEV₁ is approximately 20 mL in subjects aged 25–39 yrs, rising to 38 mL in subjects aged ≥65 yrs [38].

Few studies actually report results obtained in large samples of elderly subjects. ERICSSON and IRNELL [39], for instance, report data on 264 normal "elderly" subjects, none of whom was older than 71 yrs of age. FOWLER *et al.* [40] studied 182 Londoners aged ≥60 yrs, but only 44 subjects were aged >75 yrs and 23 were >80 yrs. ENRIGHT *et al.* [41] reported values obtained in 471 subjects aged ≥65 yrs, but only 10 males aged >80 yrs were included in the study. The two largest studies reporting spirometric data for healthy elderly subjects were published by MILNE and WILLIAMSON [42] and DUWAYNE SCHMIDT *et al.* [43]. DUWAYNE-SCHMIDT *et al.* [43] showed that FEV₁ and FVC decrease uniformly with age. Values for FEV₁/FVC were stable in young adults and then decreased for females aged >55 and males aged >60 yrs to the 70–75% range. However, MILNE and WILLIAMSON [42] noted a decrease with age for FEV₁/FVC only in females, with values remaining stable throughout the 60–90 yrs age range in males.

Reported data show that previous regression equations, based on extrapolations from groups of younger subjects, tended to overestimate predicted values for FEV₁, FVC and FEV₁/FVC in elderly subjects [42].

Peak flow and flow–volume curves

FOWLER *et al.* [40] demonstrated characteristic changes in the flow–volume curve with ageing (fig. 7). The changes in the curve suggest changes in the small peripheral

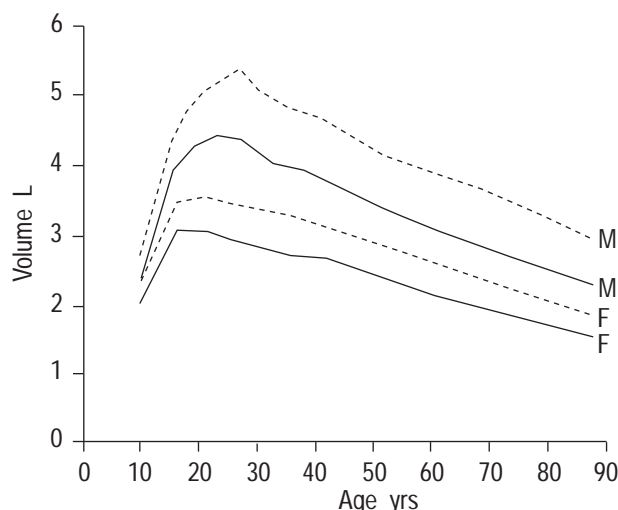


Fig. 6. – Evolution of forced expiratory volume in one second (FEV₁; —) and forced vital capacity (FVC; - - -) as a function of age. Average of data from 746 subjects free of cardiorespiratory symptoms, who had never smoked. M: males; F: females. (Adapted from KNUDSON *et al.*, 1976 [37].)

airways, with an obstructive pattern present even in lifetime nonsmokers, implying that this pattern may be normal in old age.

Peak flow rates also tend to decrease with age. The variability in predicted peak flow values is, however, very large and prediction equations are, therefore, not reliable [43]. Peak flow lability (maximal difference in peak flow/mean peak expiratory flow (PEF)) has been shown to correlate with a diagnosis of asthma in younger subjects. Although middle-aged and older persons appear to be successful in providing a measure of PEF reliably at home, older age *per se* was a factor of increased variability in longitudinal monitoring of ambulatory peak flow (independent predictor of higher PEF lability) [41]. ENRIGHT *et al.* [41] reported in a study of 1,223 subjects (mean age 66, range 43–80 yrs), a peak flow lability of $9.2 \pm 5.5\%$ for males and $8.3 \pm 4.6\%$ for females.

No specific changes have been noted regarding the inspiratory flow curves, although maximal inspiratory flow values decrease with ageing. Because lung deposition of bronchodilator or anti-inflammatory drugs is flow dependent with available powder-inhaling devices [44, 45], determination of maximal inspiratory flow in older subjects may be relevant when considering topical bronchodilator or anti-inflammatory treatment with a powder inhaler. Certain powder-inhaling devices necessitate minimal inspiratory flows of up to $60 \text{ L}\cdot\text{min}^{-1}$ and these values may not be attained in the very old. It has been shown, for instance, that with the Turbuhaler[®], lung deposition at an inspiratory flow of $30 \text{ L}\cdot\text{min}^{-1}$ is approximately half that obtained at $60 \text{ L}\cdot\text{min}^{-1}$, although still equivalent to that obtained with a metered-dose inhaler [44, 45].

Airway resistance and conductance

When adjusted for lung volume, age has no significant effect on airway resistance (R_{aw}). Peripheral airways contribute marginally to the total resistance of the airways and, therefore, changes in the peripheral airways are not reflected by changes in R_{aw} [3].

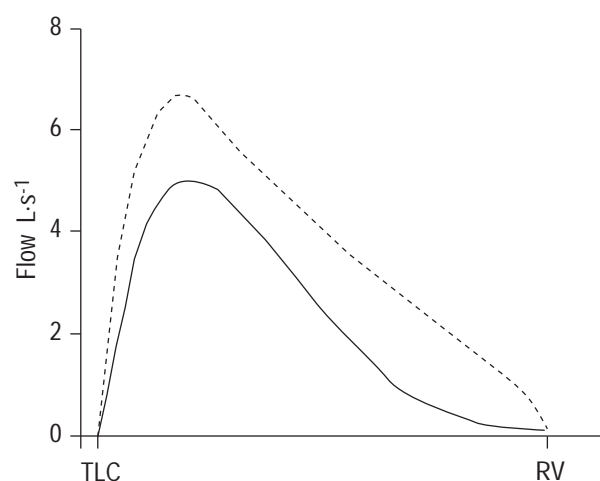


Fig. 7. – Changes in the expiratory flow–volume curve with ageing: data from 10 older subjects (mean age 71 yrs; —) and 10 younger subjects (mean age 24 yrs; - - -). TLC: total lung capacity; RV: residual volume. (Adapted from FOWLER *et al.*, 1987 [40].)

Respiratory muscles

Dysfunction of respiratory muscles may lead to hypoventilation, experienced as shortness of breath, reduced exercise tolerance and, in extreme cases, respiratory failure. The overall strength of respiratory muscles can be measured noninvasively by recording MIP and MEP at the mouth, or by measuring sniff nasal inspiratory pressure (SNIP) [46]. Both measurements can be easily performed at the bedside [47]. Inspiratory pressures are measured either at FRC or at RV. Expiratory pressures are usually measured at TLC. Values >80 cmH₂O (in males) or 70 cmH₂O (in females) for MIP, or >70 cmH₂O in males and 60 cmH₂O in females for SNIP exclude clinically relevant respiratory muscle weakness [48]. Available reference values for these measurements show a decrease with age of respiratory muscle strength (table 1). ENRIGHT *et al.* [9] measured MIP and MEP in 4,443 ambulatory subjects aged >65 yrs; their results show that normal values for females aged >65 yrs and males aged >75 yrs are below the aforementioned threshold for clinically relevant respiratory muscle dysfunction. Spirometric tests, but also nutritional status (body weight and body mass index), as well as peripheral muscle strength (handgrip) were shown to be significantly correlated with MIP and MEP values [9]. Others found values in the same range for MIP, MEP or SNIP [46, 50]. The decrease in respiratory muscle strength is likely to be relevant in elderly patients in clinical situations where an additional load is placed on the respiratory muscles, such as pneumonia [3] or left ventricular failure [21, 22].

The effects of poor nutritional status and CHF have been discussed previously.

Gas exchange

Changes in arterial oxygen tension and ventilation-perfusion relationships

WAGNER and coworkers [51, 52] have developed a technique measuring, in humans, the distribution of ventilation and perfusion, based on the simultaneous elimination by the lung of six inert gases of markedly different solubilities. This technique provides the best available overview of the distribution of ventilation and perfusion in health and disease. Using this technique, WAGNER and co-

workers [51, 52] have shown, with ageing, an increase in $V'A/Q'$ imbalance, with a rise in units with a high $V'A/Q'$ ratio (wasted ventilation or physiological dead space (V_D)) and in units with a low $V'A/Q'$ ratio (shunt or venous admixture). The decrease in P_{a,O_2} with age is a consequence of this increased heterogeneity of $V'A/Q'$ ratios and, in particular, of the increase in units with a low $V'A/Q'$ ratio (dependent parts of the lung, poorly ventilated during tidal breathing, as reflected by an increased closing volume) [51]. Regressions proposed for the computing of P_{a,O_2} as a function of age vary widely, mainly in relation to the coefficient attributed to age [53]. Indeed, for an 82-yr-old male, predicted values for P_{a,O_2} range 8.4–11.3 kPa (63–84 mmHg). GUÉNARD and MARTHAN [54] found no significant correlation between P_{a,O_2} and age in 74 subjects aged 69–104 yrs; mean values reported were 11.2 ± 1.0 kPa (84 ± 7.5 mmHg). DELCLAUX *et al.* [53] measured arterial blood gases in 274 subjects aged 65–100 yrs (mean 82 yrs) with and without airway obstruction; mean P_{a,O_2} was 10 ± 1.4 kPa (75 ± 11 mmHg). The authors suggest accepting as normal a P_{a,O_2} of 10.6–11.3 kPa (80–85 mmHg) for subjects >65 yrs of age [53].

An increase in the alveolar-arterial pressure difference for oxygen (P_{A-a,O_2}) with age would be expected because of the increase in $V'A/Q'$ heterogeneity, mostly related to the increase in closing volume. Indeed, according to SORBINI *et al.* [55], the highest normal value for the P_{A-a,O_2} at a certain age is given by the equation:

$$P_{A-a,O_2} \text{ (in mmHg)} \leq 1.4 \pm 0.43 \times \text{age (yrs)}$$

High values obtained by this equation (*i.e.* 4.8 kPa (36 mmHg) for 80 yrs of age) may be in part explained by the supine position of subjects at time of sampling. More recent studies found no significant relationship between age and P_{A-a,O_2} ; however, values reported are well above normal values for younger adults, *i.e.* 3.2 ± 1.4 kPa (24 ± 10 mmHg) [53] and 4.4 ± 0.6 kPa (33 ± 4.5 mmHg) [54].

Carbon monoxide transfer factor

Ageing is associated with a decline in the transfer capacity of the lungs for carbon monoxide ($T_{L,CO}$) [54]. The annual reduction in $T_{L,CO}$ is $0.2\text{--}0.32$ mL·min⁻¹·mmHg⁻¹ in males and $0.06\text{--}0.18$ mL·min⁻¹·mmHg⁻¹ in females [1].

Table 1. – Maximal inspiratory pressure (MIP) measured at residual volume and maximal expiratory pressures (MEP) measured at total lung capacity (cmH₂O)

Age group yrs	A		B		C		A		B		C	
	MIP [†]	n	MIP [‡]	n	MIP [‡]	n	MEP [†]	n	MEP [‡]	n	MEP [‡]	n
Males												
65–69	84	704	103±32	10			188	113	197±74	10		
70–74	81	728	103±32	10	90±25	20	179	105	185±74	10	118±39	20
75–79	74	472					161	59				
80–84	64	253					142	43				
≥85	56	102					131	9				
Females												
65–69	59	1131	70±26	10			125	176	135±40	10		
70–74	56	888	65±26	10	67±17	20	121	119	128±40	10	79±21	20
75–79	49	589					102	85				
80–84	45	243					84	34				
≥85	40	91					94	13				

A: ENRIGHT *et al.* (1994) [9]; B: BLACK *et al.* (1969) [49]; C: ULDRY and FITTING (1995) [46] (subjects were aged 66–80 yrs). [†]: means; [‡]: means±SD.

This decrease is more evident after 40 yrs of age. Incriminated factors are increased heterogeneity in \dot{V}'_A/Q' , reduction of the alveolar surface area [33, 56], decreased density of lung capillaries [57] and a decline in pulmonary capillary blood volume [54]. Although there is a considerable scatter in the results, GUÉNARD and MARTHAN [54] showed, in a population of 74 healthy subjects aged 69–104 yrs, a correlation of $T_{L,CO}$ with age:

$$(T_{L,CO} \text{ (mL}\cdot\text{min}^{-1}\cdot\text{kPa}^{-1}) = 126 - 0.9 \times \text{age (yrs); } r=0.54; p<0.001)$$

Regulation of breathing

At rest

Normal elderly subjects at rest breathe with a minute ventilation (\dot{V}'_E) identical to that of younger subjects, but with smaller tidal volumes (V_T) and higher respiratory frequencies [2]. Ageing is associated with a striking attenuation in the cardiac frequency and ventilatory responses to hypoxia and hypercapnia [58–60]. KRONENBERG and DRAGE [59] compared the hypercapnia and hypoxia responses of eight healthy young males (22–30 yrs old) with those of eight older males (64–73 yrs old). The results are shown in table 2.

Mouth occlusion pressure ($P_{0.1}$) is often used as an index of respiratory drive. It is the inspiratory pressure generated at the mouth when occluding the airway 0.1 s after the beginning of inspiration. Compared with younger subjects, the response to isocapnic hypoxia and hyperoxic hypercapnia measured by $P_{0.1}$ is reduced by about 50% for hypoxia and 60% for hypercapnia [58]. These observations suggest that there is an age-related decline in the ability to integrate information received from sensors (peripheral and central chemoreceptors and mechanoreceptors) and generate appropriate neural activity. Other studies show a diminished perception of added resistive or elastic loads with ageing [61–63]. Ageing is also associated with a decline in the ability to perceive methacholine-induced bronchoconstriction when compared with younger subjects [54].

Blunting of the response to hypoxia and hypercapnia, as well as a lower ability to perceive bronchoconstriction, represent a partial loss of important protective mechanisms (alarm signals).

During exercise

Oxygen consumption (\dot{V}'_{O_2}), expressed in $\text{L}\cdot\text{min}^{-1}$, reaches a peak between 20 and 30 yrs of age, then decreases at an estimated rate of 9% per decade [1]. The decrease is more pronounced in sedentary subjects than in those remaining physically active [64]. The Fick equation gives the relationship between cardiac output, peripheral oxygen extraction ($(C_a - C_v)O_2$) and \dot{V}'_{O_2} :

$$\dot{V}'_{O_2} = \text{cardiac output} \times (C_a - C_v)O_2$$

Factors limiting \dot{V}'_{O_2} in older subjects are reduced maximal cardiac frequency with ageing, reduced maximal cardiac output and reduced peripheral muscle mass.

In contrast to the decreased response to hypercapnia at rest, elderly subjects appear more responsive than younger subjects to CO_2 during exercise. POULIN *et al.* [65] demon-

Table 2. – Ventilatory response to hypoxia and hypercapnia in younger *versus* older subjects

	Younger subjects 22–30 yrs	Older subjects 64–73 yrs	p-value
Ventilatory response			
Hypoxia ΔV_{40} $\text{L}\cdot\text{min}^{-1}$	40.1 ± 4.7	10.2 ± 1.2	<0.001
Hypercapnia $\text{L}\cdot\text{min}^{-1}\cdot\text{mmHg}^{-1}$	3.4 ± 0.5	2.0 ± 0.2	<0.025

Data are shown as means ± SEM. ΔV_{40} : change in ventilation from initial value breathing room air to that during hypoxia (alveolar arterial oxygen tension = 40 mmHg). †: per cent change in ventilation, control (room air) to alveolar carbon dioxide tension of 55 mmHg.

strated, in a sample of 224 subjects aged 56–85 yrs that, for a given CO_2 production (\dot{V}'_{CO_2}), the ventilatory response ($\dot{V}'_E/\dot{V}'_{CO_2}$) increases with ageing. This response was not related to oxygen desaturation or increased metabolic acidosis. A possible explanation is a higher \dot{V}_D/V_T in the elderly subjects tested. In agreement with this hypothesis is the observation of a higher difference between end-tidal (P_{ET,CO_2}) and arterial carbon dioxide tensions (P_{a,CO_2}) in older subjects, and the increase in \dot{V}'_A/Q' heterogeneity with ageing described previously. In itself, this may increase dyspnoea for a given workload. Indeed, for a given \dot{V}'_E , the oxygen cost of breathing is higher in elderly subjects.

During sleep

The prevalence of sleep-disordered breathing increases in elderly subjects. In middle-aged populations, the prevalence of the sleep apnoea syndrome (using an apnoea/hypopnoea index (AHI) 15 events·h⁻¹ as a cut-off value) is estimated to be 4% in females and 9% in males [66], whereas repetitive episodes of upper airway obstruction have been estimated to occur in 24–75% of elderly subjects [67]. Even when higher cut-off values are used (*i.e.* AHI ≥ 20), the prevalence of the sleep apnoea syndrome in the elderly is reportedly as high as 44%. Sleep-disordered breathing may be associated with impairment in cognitive function [68] and is reported to be more frequent in Alzheimer's disease. Interestingly, respiratory effort in response to upper airway occlusion in elderly patients is decreased compared with younger subjects [69].

Age-related difficulties and limitations in performing pulmonary function tests

Although performing pulmonary function tests in outpatients aged >65 yrs appears feasible in 90% of subjects [70], the situation is quite different in institutionalized or hospitalized elderly patients because of a higher prevalence of cognitive impairment. The prevalence of delirium in older people on admission to hospital ranges 10–24%, whereas delirium develops in 5–32% of older patients after admission [63]. The reported prevalence of dementia before the age of 75 yrs is 2.9%, but rises to 5.6% after 75 yrs and 22% after 80 yrs [71]. In this group of subjects, CARVALHAES-NETO *et al.* [72] showed that measuring the impedance of the respiratory system can be performed in

patients with moderate to severe cognitive impairment, allowing airway obstruction to be identified and quantified. The use of SNIP may also be simpler in this age group than measuring mouth inspiratory pressures. Plethysmographic measurement of lung volumes is seldom required in this age group.

Conclusions

Physiological ageing of the respiratory system is associated with changes in the compliance of the chest wall and lung parenchyma, which result in static air-trapping, increased functional residual capacity and increased work of breathing. Expiratory flow rates decrease with ageing, with characteristic changes in the flow–volume curves suggesting increased collapsibility of peripheral airways. Respiratory muscle function is affected by geometric changes in the rib cage and is strongly correlated with nutritional status (lean body mass, body weight), peripheral muscle mass and strength and cardiac index. In subjects aged ≥ 80 yrs, values of maximal inspiratory pressure may reach critically low values, which may be associated with alveolar hypoventilation in circumstances such as left-sided heart failure or pneumonia. Gas exchange is well preserved at rest and during exertion in spite of a reduced alveolar surface area and increased ventilation–perfusion heterogeneity. In fact, in elderly subjects with regular training, the respiratory system can adapt to high levels of exercise. However, age-associated alterations of the respiratory system tend to diminish the subjects' reserve in cases of infection or heart failure. Decreased sensitivity of respiratory centres to hypoxia or hypercapnia will result in a diminished ventilatory response in cases of acute disease such as heart failure, infection or aggravated airway obstruction. Furthermore, decreased perception of added resistive loads (*i.e.* bronchoconstriction) and diminished physical activity may result in less awareness of the disease and delayed diagnosis.

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