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Arterial blood gases in elderly persons with chronic obstructive pulmonary disease (COPD)

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Arterial blood gases in elderly persons with chronic obstructive pulmonary disease (COPD). B. Delclaux, B. Orcel, B. Housset, W.A. Whitelaw, J-P. Derenne. © ERS Journals Ltd 1994.

ABSTRACT: With the increasing number of elderly people in developed countries, physicians are often confronted with patients whose arterial oxygen tension, Pa_{O_2}, is lower than that of normal young adults. The normal values predicted in the literature for very old individuals are generally extrapolated from younger subjects. The purpose of the present study was to obtain Pa_{O_2} values from a large population of elderly subjects with normal and obstructive ventilatory function.

We measured arterial blood gases in 274 subjects, aged 65–100 yrs (mean 82 yrs), with chronic bronchitis and moderate airways obstruction (mean forced expiratory volume in one second (FEV_1), 53% pred).

Mean Pa_{O_2} was 10.0±1.4 kPa (75.2±10.8 mmHg) and mean arterial carbon dioxide tension (Pa_{CO_2}) was 5.4±0.8 kPa (40.5±6.1 mmHg). Both Pa_{O_2} and Pa_{CO_2} were independent of age. Blood gas abnormalities were associated with airways obstruction: Pa_{O_2} was positively correlated to FEV_1 and Pa_{CO_2} was negatively correlated to FEV_1. Pa_{O_2} was 10.8±1.4 kPa (81.5±10.7 mmHg) in the patients with FEV_1 ≥90% predicted *versus* 9.5±1.3 kPa (71.5±10.1 mmHg) in those with FEV_1 ≤35% pred.

These findings suggest that the predicted Pa_{O_2} extrapolated from younger normal values are often erroneously underestimated. It is probably more accurate to accept as normal a Pa_{O_2} of 10.6–11.3 kPa (80–85 mmHg) for all subjects over 65 yrs, irrespective of their age.

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Blood gases are often measured as part of respiratory assessment. With the increasing number of elderly people in developed countries, physicians are often confronted with patients whose arterial oxygen tension (Pa_{O_2}) is lower than that of normal young adults. Deciding whether they are normal or not depends on the comparison with "normal" values for elderly persons.

Pa_{O_2} decreases from youth to middle age as shown in many studies, but very few individuals over the age of 60–70 yrs have been included in previous series [1–13] (table 1), so that the "normal" Pa_{O_2} values given for elderly subjects are an extrapolation from linear regression equations. However, it has been suggested that such predictions may be in error because, in fact, the Pa_{O_2} of very old subjects may not be much different from Pa_{O_2} of individuals of 65 yrs [13].

We present the blood gas data for a population of very old patients with moderate chronic airways obstruction and show that their Pa_{O_2} values are somewhat higher than would be expected if Pa_{O_2} had continued to decline with age past the sixth decade. The results are important for clinicians who use blood gases as a help in deciding whether patients are acutely ill.

Patients and methods

Patient population

The study was performed on 281 elderly persons from 24 nursing homes and hospitals for chronic disabled patients. They had all been in these institutions for at least one year, unable to care for themselves for various social and medical reasons. All of them satisfied the criteria for chronic bronchitis, *i.e.* a history of excessive sputum expectoration occurring on most days during at least 3 consecutive months for not less than 2 consecutive years [14]. At least four episodes of exacerbation of chronic bronchitis requiring antibiotic treatment had occurred in each patient during a 6 month reference period (October 1986 to April 1987) in the previous year. Patients were excluded if, on the basis of clinical examination and review of chest X-rays, they were considered to have any cardiopulmonary disease except chronic bronchitis. There were 72 smokers, 71 ex-smokers and 137 nonsmokers. The smokers were younger (78±8 yrs) than the ex-smokers (83±8 yrs) and

Table 1. – Effects of age on arterial blood gases according to previous studies

Authors [Ref]	Subject	Age#	Age ≥60 yrs	Age ≥70 yrs	Pa_{O_2} *versus* age		Predicted Pa_{O_2} at age 82 yrs		r	p	Pa_{CO_2}##	
	n	yrs	n	n	kPa	mmHg	kPa	mmHg			kPa	mmHg
LOEW and THEWS [2]			29	?			8.9	67*				
RAINE and BISHOP [5]	70	17–66	?		13.8 - 0.032 age	103.7 - 0.24 age	11.2	84*	0.38	<0.01		
CONWAY *et al.* [6]	70	48	11	2	13.7 - 0.029 age	102.5 - 0.22 age	11.3	84.4*			5.1±0.4	38.6±3.1
MELLEMGAARD [7]	80	41±17	12	?	13.9 - 0.036 age	104.2 - 0.27 age	10.9	82*	0.56	<0.001	5.1±0.4	38.4±2.9
SORBINI *et al.* [8]	152	18–84	24	?	14.5 - 0.057 age	109.0 - 0.43 age	9.8	73.7*	0.91	<0.001		
DIAMENT and PALMER [9]	65M	43±17	?	?	14.6 - 0.041 age	109.5 - 0.31 age	11.2	83.9*			5.4±0.5	40.9±3.6
	86F	45±16	?	?	15.3 - 0.055 age	114.8 - 0.41 age	10.8	81.1*			5.2±0.5	39.0±3.8
HERTLE *et al.* [10]	323	42±16	26	11	12.8 - 0.053 age	96.2 - 0.40 age	8.4	63.3*				
GOTHGEN and JACOBSEN [12]	20	19–80	8	4	13.8 - 0.053 age	103.5 - 0.40 age	9.4	70.3*				

#: range or mean±SD; ##: mean±SD; *: extrapolated from figure 2. Pa_{O_2}: arterial oxygen tension; Pa_{CO_2}: arterial carbon dioxide tension. M: male; F: female.

the nonsmokers (84±7 yrs). Most of the men were smokers or ex-smokers and most women were nonsmokers. Sex ratio M/F was 53/18, 56/14 and 19/113 in the three groups respectively. Smoking status was unknown in one patient.

Ethics

All patients gave verbal consent after having the purpose of the study described by the physician in charge of the trial in the presence of a third party. The study was approved by the Ethics Committee of the Saint Antoine Faculty of Medicine (Paris).

Measurement principles and techniques

A single medical investigator visited each institution and set up a portable laboratory. Arterial blood gases (Pa_{O_2}), and arterial carbon dioxide tension (Pa_{CO_2}) were measured on patients at rest, sitting or semi-recumbent, and breathing room air. Arterial blood samples were obtained in a disposable pre-heparinized system from the radial or brachial artery and processed in less than 5 min in a Corning 178 blood gas analyser.

The latter was calibrated twice a day using standard gas mixtures. Since it has been shown that the state of activity influences blood gas measurements [13], the patients rested for more than 10–15 min before blood samples were taken. After testing, four were excluded because of hyperventilation (pH >7.50), and three others because of uncompensated acidosis (pH <7.34). Therefore, the population analysed was 274 (128 men and 146 women). Mean age was 82±8 yrs (range 65–100 yrs); mean weight was 59±13 kg; mean height was 161±9 cm. Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured with a portable spirometer (Fukuda Sanyo Spiro Analyser ST 90). The patients were first shown how to make a forced expiration. After one or two training manoeuvres without the apparatus, they made a series of 2–4 forced expirations. The best values were kept for analysis. The predicted values were taken from QUANJER [15].

Statistical methods

Values are expressed as mean±standard deviation. Analysis of correlations was performed by the method of least squares. Correlations were established between each parameter and age, and between Pa_{O_2}, Pa_{CO_2} and spirometric measures. Statistical significance was accepted at the 95% confidence level ($p<0.05$).

Results

Mean Pa_{O_2}, Pa_{CO_2} and alveolar-arterial gradient for oxygen (P_A-a_{O_2}) for the whole group were 10.0±1.4 kPa (75.2±10.8 mmHg), 5.4±0.8 kPa (40.5±6.1 mmHg)

and 3.2±1.4 kPa (24.3±10.3 mmHg), respectively. $Paco_2$ was between 6.1–6.7 kPa (46–50 mmHg) in 31 patients and above 6.7 kPa (50 mmHg) in 14.

Pao_2, $Paco_2$ and P_{A}-ao_2 were essentially similar in men (mean age 81 yrs) and women (mean age 83 yrs). Mean Pao_2 values were 10.1 kPa (75.9 mmHg) and 9.9 kPa (74.5 mmHg); $Paco_2$ 5.3 kPa (40.2 mmHg) and 5.4 kPa (40.7 mmHg); and P_{A}-ao_2 3.2 kPa (23.9 mmHg) and 3.3 kPa (24.6 mmHg), respectively. The individual values for Pao_2 and $Paco_2$ as a function of age are shown in figure 1a and b. Pao_2 did not decrease with age. It was independent of age in men. It was positively correlated in women, but the correlation was weak: r=0.18; p<0.05. $Paco_2$ was independent of age. P_{A}-ao_2 was negatively correlated to Pao_2 (r=-0.74; p<0.001) and to $Paco_2$ (r=-0.30; p<0.001).

Mean FEV_1 was 1.0±0.5 *l* (53±24% pred). Mean FVC was 1.6±0.7 *l* (62±24% pred). Mean FEV_1/FVC was 67±18%.

There were significant correlations between blood gases and spirometric parameters. Pao_2 was positively correlated to FEV_1 (fig. 1c). $Paco_2$ was negatively correlated to FEV_1 (fig. 1d) and to Pao_2: $Paco_2$ kPa = 7.77 - 0.24 Pao_2 ($Paco_2$ mmHg = 58.4 - 0.24 Pao_2) (r=-0.42; p<0.001). The correlation coefficients between blood gases (Pao_2 and $Paco_2$) and FEV_1 expressed as % predicted values were 0.28 (p<0.001) and 0.39 (p<0.001). FVC was not correlated to $Paco_2$ and Pao_2. FEV_1/FVC was positively correlated to Pao_2 (r=0.29; p<0.001) and negatively to $Paco_2$ (r=-0.31; p<0.001).

In the patients with the more severe impairment in blood gases (Pao_2 <8 kPa or $Paco_2$ ≥6.12 kPa) there was no correlation between FEV_1 and $Paco_2$, and Pao_2 was positively but weakly correlated to FEV_1 (r=0.14; p<0.05).

Blood gases in the patients with the most severe airways obstruction (FEV_1 ≤35% pred) and in those with normal values (FEV_1 >90% pred) are shown in table 2. Mean Pao_2 was significantly lower and $Paco_2$ significantly higher in the patients with the more advanced disease. FEV_1 (% pred) was 43±17 in the patients with $Paco_2$ 6.1–6.7 kPa (46–50 mmHg) and 25±7 in those with $Paco_2$ >6.7 kPa (50 mmHg). Those values were significantly smaller than in the other patients.

Smoking status had little influence on blood gases and spirometric measurements. For the three groups (smokers, ex-smokers and nonsmokers), Pao_2 was 10.1±1.5 kPa (75.8±11.1 mmHg), 10.3±1.5 kPa (76.9±10.9 mmHg) and 9.9±1.4 kPa (74±10.5 mmHg); $Paco_2$ was 5.6±0.9

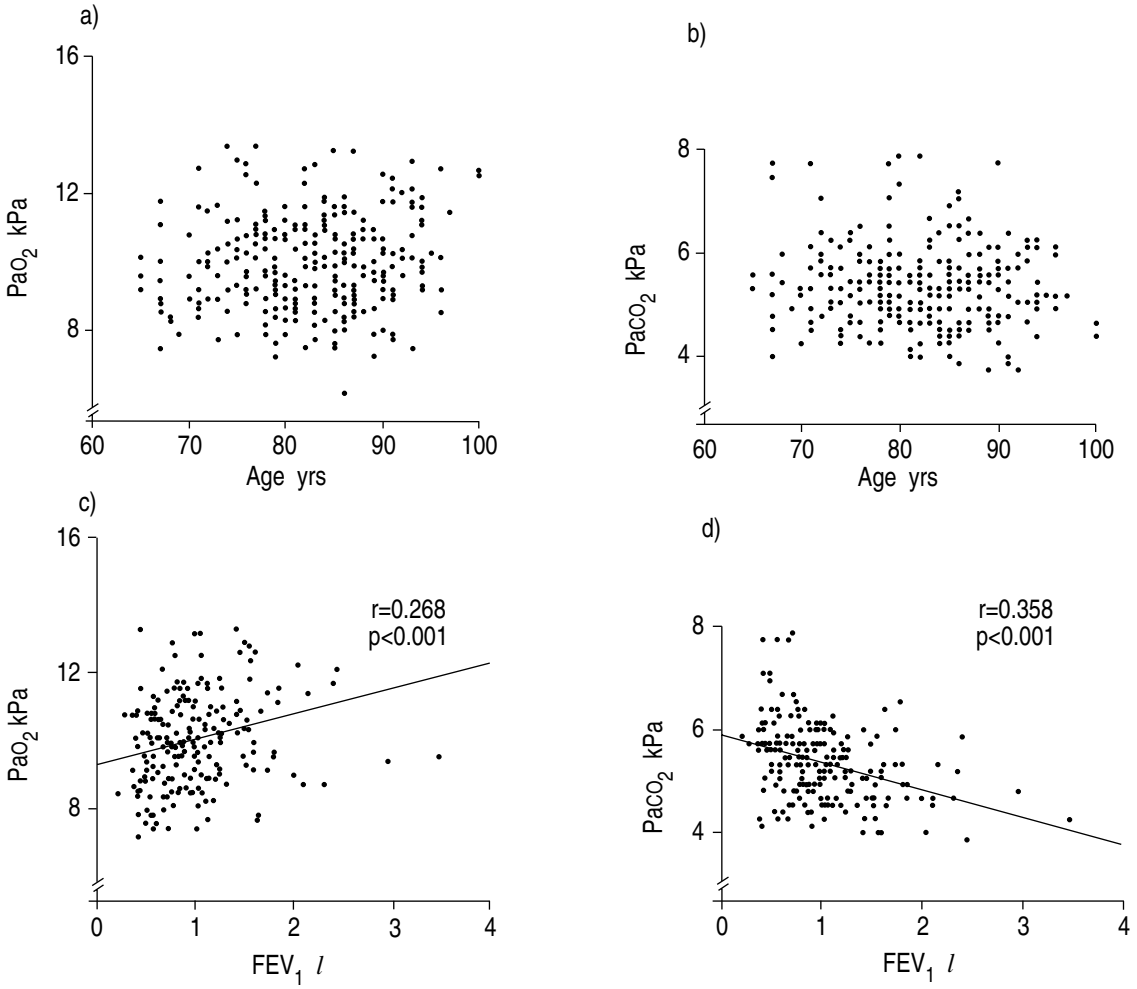

Fig. 1. – a) Pao_2 and b) $Paco_2$ as a function of age. There was no correlation between arterial blood gases and age. c) Pao_2 was positively correlated to FEV_1 d) $Paco_2$ was negatively correlated to FEV_1. Pao_2: arterial oxygen tension; $Paco_2$: arterial carbon dioxide tension; FEV_1: forced expiratory volume in one second. (1 mmHg=0.133 kPa).

Table 2. – Arterial blood gases in patients with and without severe airways obstruction

Patients groups	Patients n	Sex M/F	Age# yrs	FEV_1# %pred	Pa_{O_2}# kPa (mmHg)	Pa_{CO_2}# kPa (mmHg)
FEV_1 ≥90% pred	15	6/9	84±10	108±19	10.8±1.4 (81.5±10.7)	4.8±0.6 (35.9±4.4)
FEV_1 ≤35% pred	51	29/22	80±7	27±6	9.5±1.3 (71.5±10.1)	5.7±0.9 (43.2±6.6)

#: data are presented as mean±SD. FEV_1: forced expiratory volume in one second. For further abbreviations see legend to table 1.

kPa (41.8±6.5 mmHg), 5.2±0.7 kPa (38.8±5.6 mmHg) and 5.4±0.8 kPa (40.6±6 mmHg); $P_{A\text{-}a}O_2$ was 2.9±1.2 kPa (22±9.3 mmHg), 3.3±1.4 kPa (24.7±10.6 mmHg) and 3.4±1.4 kPa (25.3±10.4 mmHg). There were no significant differences between the three groups for any of these parameters. The nonsmokers had smaller FEV_1 but this difference disappeared when corrected for height and sex. The smokers were younger and had smaller FEV_1 (expressed as % predicted) and FEV_1/FVC.

On average, our patients were not overweight. Mean body mass index (BMI) was 22.8±4.6 and mean ratio body weight/ideal body weight (BW/IBW) was 1.03± 0.21. Pa_{CO_2} was not correlated with BMI and BW/IBW. Pa_{O_2} was negatively correlated with both, but the correlation was weak: r=-0.14 and -0.15 ($p<0.05$, for each).

Discussion

The patients described in this study are fairly typical of moderate chronic airways obstruction with reduced FEV_1 and FVC, chronic cough with expectoration and frequent episodes of apparent infection, leading their physicians to prescribe antibiotics. However, some patients had a moderate restrictive ventilatory defect or a combined restrictive and obstructive ventilatory defect. Since patients with clinical signs or chest X-ray pattern suggesting an interstitial lung disease have been excluded, the likely explanation for this condition in this type of population is the presence of kyphosis and/or muscle weakness. In fact, they were living in nursing homes for a variety of reasons, some because of respiratory disability but others because of immobility due to other diseases, decreasing cerebral function, or for social reasons. At the time of the measurements, they were not suffering from acute respiratory events. They thus represent a reasonable sample of institutionalized elderly persons with moderate chronic obstructive pulmonary disease (COPD) in baseline conditions. Although some may have had sleep apnoea or chronic sedative overdose, it is likely most of the cases of hypercapnia can be attributed mainly to COPD, implying that there were numerous advanced cases in the group. In fact, Pa_{CO_2} was higher in patients with low FEV_1, and FEV_1 was lower in those with hypercapnia. This suggestion is supported by the negative correlation between Pa_{CO_2} and FEV_1 and FVC: the worse the obstruction the worse the hypercapnia. On the other hand, Pa_{CO_2} was not correlated with age, which is in agreement with most reports [16].

Patients with COPD in stable conditions can be expected on average to have an increased alveolar-arterial gradient for oxygen and a decrease in Pa_{O_2} due to the disease itself, and therefore to have lower Pa_{O_2} than comparable persons with healthy lungs. In our series, this supposition is borne out by finding a positive correlation between FEV_1 and Pa_{O_2}. The worse the obstruction, the lower the oxygen. However, airway obstruction in itself is not the only determinant of blood gases, and several patterns of ventilation-perfusion inequality have been described in COPD patients [17].

A correlation between FEV_1 and Pa_{O_2} has been found among younger patients with chronic obstructive airways disease by PALMER and DIAMENT [18], who studied a group of patients with mean age 60 yrs and obtained a regression giving Pa_{O_2} 7.58±2.13 kPa (57±16 mmHg) - FEV_1 *l*. As with their population, however, the scatter in our data was such that Pa_{O_2} in any one patient could be of little use in evaluating the severity of obstruction.

In searching the literature for normal values of blood gases in old people we found 13 published articles [1–13] describing the relationship between Pa_{O_2}, Pa_{CO_2} and age in populations of normal people. In addition, STANESCU *et al*. [19] reported a mean arterial oxygen saturation of 96% in 23 normal subjects aged 61–86 yrs (mean 71 yrs). Seven of them, listed in table 1, calculated linear regressions of Pa_{O_2} and Pa_{CO_2} against age for sitting subjects. The studies of DIAMENT and PALMER [9] and RAINE and BISHOP [5] included both smokers and nonsmokers. The regression lines of these series are shown in figure 2 together with our own. In addition, our patients with normal FEV_1 and those with more severe airways obstruction are illustrated separately.

If the regression lines, which had negative slopes ranging from 0.22–0.43 mmHg per year, are followed to age 82 yrs the mean age of our population, the various studies give predictions for normal Pa_{O_2} ranging from 8.4–11.2 kPa (63.3–84.4 mmHg). The largest series, that of HERTLE *et al*. [10], predicted a normal value of 8.4 kPa (63.3 mmHg), well below the mean value of our subjects with chronic bronchitis of 10.0 kPa (75.2 mmHg). The second largest series, that of SORBINI *et al*. [8], predicted 9.8 kPa (73.7 mmHg). These predictions are close to the measured values of Pa_{O_2} in those of our patients with the most severe airways obstruction (table 2 and fig. 2), and must be in error. On the other hand, the large series

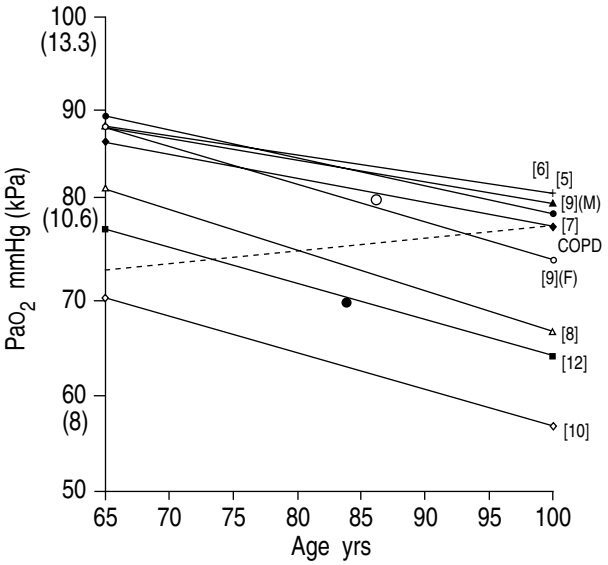

Fig. 2. – Pa_{O_2} predicted for old people from extrapolations of regression lines of younger subjects in the literature indicated by their reference numbers [5–10, 12], all show negative slopes. The regression lines of the Pa_{O_2} measured in our COPD patients (- - -) are independent of age. O: mean of 15 patients with FEV_1 ≥90% predicted. ●: mean of 51 patients with FEV_1 ≤35% predicted. (1 mmHg=0.133 kPa).

of DIAMENT and PALMER [9], and the somewhat smaller ones of CONWAY *et al*. [6], MELLEMGAARD [7] and RAINE and BISHOP [5] predicted a Pa_{O_2} between 10.9–11.2 kPa (82–84.4 mmHg) at age 82 yrs, which seems more reasonable by comparison with the values obtained in our patients with COPD.

Differences between the slopes and intercepts of the Pa_{O_2}-age relationships reported by various authors may reflect different populations of normals, sampling bias, differences in measurement techniques, or simply statistical variations. None of them report confidence intervals on their estimates of regression coefficients. Concerning their estimates of values of Pa_{O_2} and Pa_{CO_2} in very old individuals, it is important to note that their samples included few subjects over 60 yrs and even fewer over 70 yrs (table 1). Their predicted equations, thus, require the assumption that Pa_{O_2} declines at exactly the same rate throughout life, from 20–100 yrs.

The study of BLOM *et al*. [13] suggests that Pa_{O_2} in normal subjects does not, in fact, decline after 70 yrs. They presented the results of measurements in 111 persons in the form of a moving average of Pa_{O_2} on age, and showed a descending limb followed by an ascending plateau in the patients >70 yrs.

Lack of decline of Pa_{O_2} with age in elderly people could be explained in several ways. Loss of mechanical function may become less rapid in old age, or the relationship between changes in airways and pulmonary vessels with age may be such that ventilation-perfusion matching does not deteriorate in this age range. In cross-sectional studies, however, another explanation is that the subjects with the lower Pa_{O_2} may have disappeared from the sample population. This possibility was suggested by BLOM *et al*. [13] for their population of normals. It is even more plausible as an explanation for the lack of decline of mean Pa_{O_2} with age in our population of COPD patients. In a population of patients with chronic airways obstruction, life expectancy is strongly dependent on the severity of blood gas abnormalities [20]. When significant hypoxaemia and hypercapnia are present, a majority of patients will die in a few years. The natural history of such patients in the later stages of disease, as Pa_{CO_2} begins to rise, is that FEV_1 declines steadily and Pa_{O_2} declines slowly at first, then rather rapidly shortly before the patient dies. A cross-sectional study can, therefore, be expected to have few patients with low values of Pa_{O_2}. Thus, it is unlikely that our population of very old patients had been hypoxaemic for a long time. Whether these long survivors are exceptionally "healthy" subjects or are more like "normal" subjects, is debatable. Whatever the reason, our data indicate that Pa_{O_2} in these patients is surprisingly high.

From a clinical point of view, this study points out that some of the published normal values for Pa_{O_2} based on linear regressions with age cannot be relied upon for aged patients. Values predicted as normal by some equations [8, 10, 12], in fact, probably indicate a considerable gas exchange abnormality. Whilst there is not yet enough data to be certain, it is probably more accurate to accept as normal a Pa_{O_2} of 10.6–11.3 kPa (80–85 mmHg) for all subjects over 65yrs, irrespective of their age. Our data indicate that very old patients with moderate COPD have Pa_{O_2} values that are surprisingly close to normal. A very low Pa_{O_2} in such patients cannot be safely attributed to age or to chronic airway disease, but should alert the clinician about the possibility of some additional acute or chronic respiratory problem.

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