ORIGINAL ARTICLE

DIFFERENCES BETWEEN FINNISH AND EUROPEAN REFERENCE VALUES FOR PULMONARY DIFFUSING CAPACITY

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ABSTRACT

Objectives. To compare European (ECSC) and Finnish reference values for single-breath diffusing capacity for carbon monoxide (DL_{CO}).
Study design. Finnish reference values for DL_{CO}, specific diffusing capacity (DL_{CO}/VA) and total lung capacity (TLC) were compared with ECSC reference values calculated for different age, height and weight groups. In addition, 10 healthy subjects performed the test with both the Finnish method (inhaled volume 90% of vital capacity, VC) and the ECSC method (inhaled volume 100% of VC).
Methods. Percentual differences between the ECSC and Finnish reference values for DL_{CO}, TLC and DL_{CO}/VA were calculated. The results of measurements of DL_{CO} and TLC by using inhaled volume of 100% of VC and 90% of VC in 10 healthy subjects were compared.
Results. The Finnish DL_{CO} reference value for men was 3–12% and for women 8–20% smaller than the ECSC reference value. TLC calculated according to Finnish equations was 2–14% greater than that based on ECSC equations. The ECSC reference value for DL_{CO}/VA was about 20% greater than the Finnish reference value in men and 30% greater than that in women. The 10 healthy subjects had significantly higher DL_{CO} when measured according to the ECSC method as compared with the Finnish one ($p<0.004$).
Conclusions. The Finnish reference values for DL_{CO} were about 10% smaller, but TLC 10% and DL_{CO}/VA 20-30% greater than ECSC reference values in subjects of the same age, height, weight and gender. The difference in DL_{CO} is explained by the different inhaled lung volumes used in the two methods, the difference in lung volumes probably arising from ethnic differences in thoracic cavity. *(Int J Circumpolar Health 2007; 66(5): 449-457)*

Keywords: diffusing capacity, total lung capacity, ethnic differences, Finnish, Sami, middle European

INTRODUCTION

In several human races, lung volume relative to height is smaller than in Europeans. The smallest height-related lung volume is in African Blacks and East Indians, and the largest in Scandinavians and inhabitants of the Highlands (1,2). Ethnic differences are nowadays being corrected for forced expiratory volume in one second (FEV1) and for forced vital capacity (FVC) according to international recommendations (1,3).

Diffusing capacity of the lungs (DL_{CO}) is used to assess the condition of lung tissue in several pulmonary diseases, for example, emphysema, alveolitis or other diseases of lung parenchyma. DL_{CO} is usually measured with an indicator gas containing a small concentration of carbon monoxide (CO) in inhaled air to represent the gas exchange capacity of lung tissue, which is almost independent of ethnic origin (1,4,5). African Blacks may have a relatively low height-standardized diffusing capacity (6,7), as opposed to those from high altitudes, with a relatively high diffusing capacity (8–10), but good comparisons are lacking. Differences in diffusing capacity between different races are, however, anticipated to be minimal, which is why no correction has been recommended (1,11–13).

During diffusing capacity measurement, lung volumes, total lung capacity (TLC) and residual volume (RV) are measured based on gas dilution. The relation of total diffusing capacity to alveolar volume (volume approaching TLC) is called specific diffusing capacity (DL_{CO}/VA). Height-related TLC varies ethnically similarly to lung volumes measured in spirometry (3,14).

Finland is a nation situated in Scandinavia, and extends from the Gulf of Finland in the south (bordering the Baltic Sea) to Lapland in the north. Reference values based on the Finnish population are used for spirometry and diffusing capacity evaluations. When we compared Finnish reference values (15) of spirometric volumes with central European ones – the so-called European Community for Steel and Coal (ECSC) reference values (11,16) – we found the Finnish values to be 10–20% greater (17). Larger lung volumes in Finns than in middle Europeans may have a genetic basis. Differences in lung volumes might influence the specific diffusing capacity values. Thus, the use of Finnish reference values could potentially lead to misinterpretations of non-Finnish subjects' diffusing capacity results. Today, non-Finnish subjects are relatively common clients in the Finnish health care system.

Our aim was to compare Finnish and ECSC reference values for diffusing capacity and static lung volumes measured with a single-breath diffusing capacity method to determine whether a correction is needed when non-Finnish subjects are studied in Finland, or when Finns are studied in central Europe.

MATERIAL AND METHODS

Comparison of reference values

We calculated reference values for DL_{CO} for men with a height of 180 cm and women with a height of 165 cm, DL_{CO}/VA for men with a height of 180 cm and a weight of 80 kg and women with a height of 165 cm and

a weight of 60 kg, and TLC for men with a height of 180 cm and a weight of 80 kg and women with a height of 165 cm and a weight of 60 kg, with ages ranging from 20 to 70 years according to Finnish (14) and ECSC (11,15) regression formulae.

ECSC reference values (11,15):
men: DL_{CO} = 1.11x height-0.66 x age-6.03
women: DL_{CO} = 8.18 x height-0.049 x age-2.74
men: TLC=7.99 x height-7.08
women: TLC=6.60 x height-5.79
for both sexes:
specific diffusing capacity=DL_{CO}/TLC

Finnish reference values (14):
log f=b1A+b2 logA+b3/H+b4/W+1

The regression coefficients b1, b2, b3 and b4 for DL_{CO}, DL_{CO}/VA and TLC are reported in the reference publication (14) (A=age, H=height, W=weight). Calculation of the DL_{CO} reference value is made according to age and height; in calculation of TLC and DL_{CO}/VA reference values weight is also used.

The percentual difference was obtained when the ECSC reference value was subtracted from the Finnish one and the difference was divided by the ESCS reference value.

Analysis of effect of methods on diffusing capacity results

DL_{CO}, VC, TLC and DL_{CO}/VA were measured for 10 healthy non-smoking volunteers working at the hospital (9 women and 1 man, age 48.7±12.8 y [mean and SD; range 21-69 y], height 165.3±5.2 cm, weight 69.5±9.3 kg) based on the Finnish method (14) with the patient inhaling 90% of VC and on the ECSC method with the patient inhaling 100% of VC. The diffusing capacity and volume results obtained by both methods were compared with each other with paired t-test.

The study protocol was approved by the Ethics Committee of Internal Medicine of the Hospital District of Helsinki and Uusimaa, and informed consent was signed by all volunteers.

RESULTS

Comparison of reference values

The ECSC reference value for DL_{CO} was usually higher than the Finnish reference value, and this was particularly true in women (Fig. 1). By contrast, in short men the Finnish reference value was higher than the ECSC reference value.

The Finnish reference value for TLC was higher in men and women than the ECSC reference value (Fig. 2).

The Finnish reference value for DL_{CO}/VA for men was lower (at its lowest, 22% lower) than that calculated according to the ECSC reference equation. In women, the Finnish DL_{CO}/VA reference value was 27–33% smaller than the ECSC reference value (Fig. 3).

Comparison of methods

TLC value was similar, but the DLco result was significantly lower (mean 3.46%, SD 3.09, range -1.2 – +9.4%), when the single-breath test was performed with the Finnish method than when performed with the ECSC method (Table I).

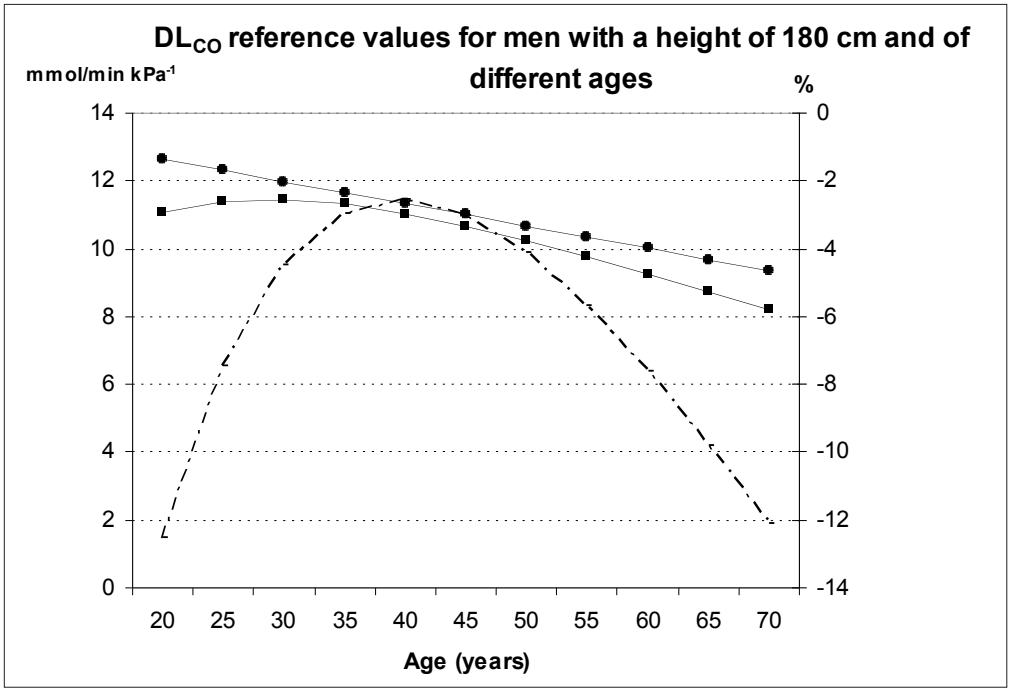

Figure 1 a). Comparison of ECSC (–●–) and Finnish (–■–) reference values for DL_{CO} in men of different ages. The difference between reference values is indicated with ---.

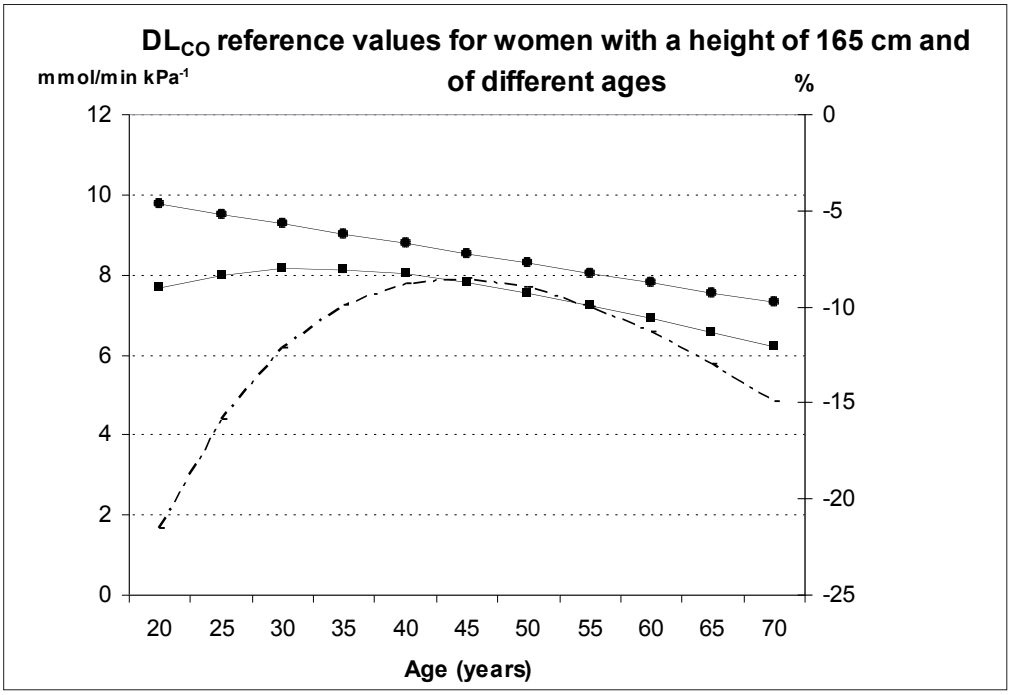

Figure 1 b). Comparison of ECSC (–●–) and Finnish (–■–) reference values for DL_{CO} in women of different ages. The difference between reference values is indicated with ---.

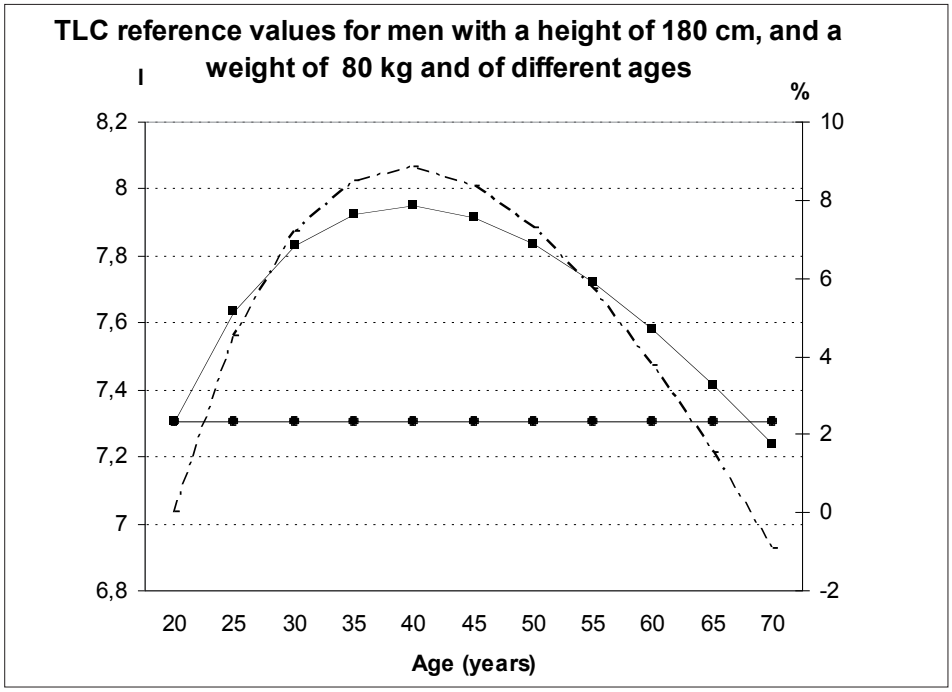

Figure 2 a). Comparison of ECSC (–●–) and Finnish (–■–) reference values for TLC in men of different ages, heights and weights. The difference between the reference values is indicated with ---.

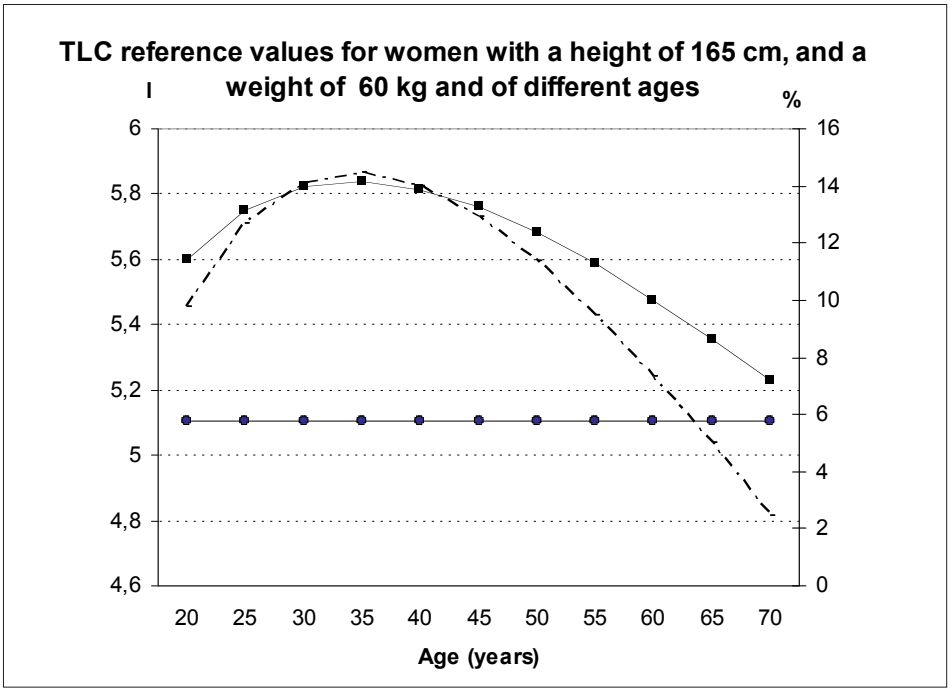

Figure 2 b). Comparison of ECSC (–●–) and Finnish (–■–) reference values for TLC in women of different ages, heights and weights. The difference between the reference values is indicated with ---.

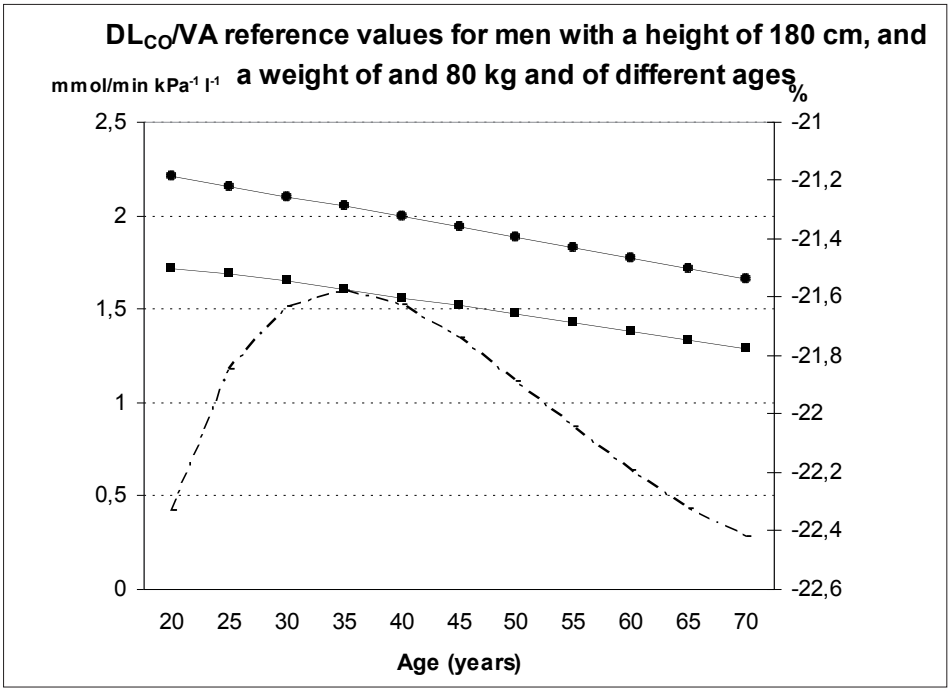

Figure 3 a). Comparison of ECSC (–●–) and Finnish (–■–) reference values for DL_{CO}/VA in men of different ages, heights and weights. The difference between reference values is indicated with ---.

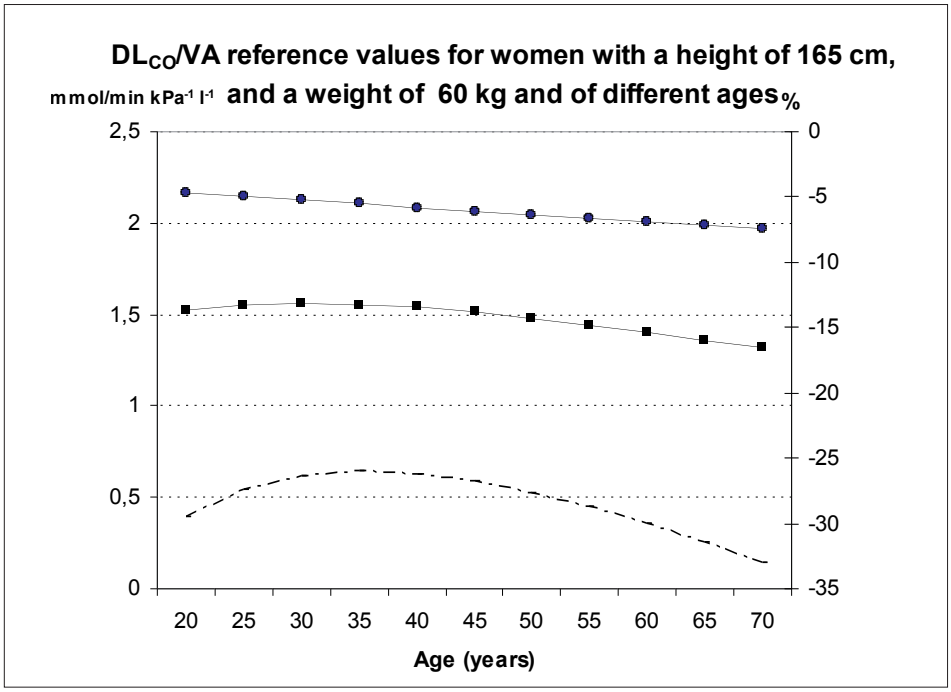

Figure 3 b). Comparison of ECSC (–●–) and Finnish (–■–) reference values for DL_{CO}/VA in women of different ages, heights and weights. The difference between reference values is indicated with ---.

Table I. Diffusing capacity measurement was performed twice for 10 healthy subjects. In one examination, the inspired volume (Vin) was 100% of maximal vital capacity (ECSC method) and in the other 90% of maximal vital capacity (Finnish method). The order of the measurements was random.

	VC (l) ECSC	VC (l) Finnish	Vin 100% of VC ECSC	Vin 90% of VC Finnish	TLC (l) ECSC	TLC (l) Finnish	DL_{CO} (mmol/min/kPa) ECSC	DL_{CO} (mmol/min/kPa) Finnish
Mean	3.81	3.83	3.74	3.44	5.27	5.3	7.06	6.82
Standard Deviation	0.72	0.77	0.70	0.69	0.65	0.69	1.44	1.39
p-value*	ns		<0.0001		ns		<0.004	

VC = vital capacity, Vin = inspired volume, TLC = total lung capacity, DL_{CO} = diffusing capacity. *paired t-test

DISCUSSION

The Finnish reference value for TLC was higher than the ECSC reference value, as in an earlier study reporting reference values for FVC or FEV1 (17). The greater TLC values probably arise from differences in the thoracic cavity volume; the relation of the body and legs to the height of a person varies in different races (1,4,5). The ethnic differences may be genetic in origin. However, environmental factors might also explain the greater lung volume in Finns than in central Europeans. Increased habitual activity because of a cold climate as well as training of muscles in activities increasing inspiratory capacity, for example, skiing and swimming (1), may also have influenced the development of larger lung volume in Finns.

As the age- and height-related Finnish TLC reference values were greater than the ECSC reference value, one could assume that also the Finnish reference value for DL_{CO} would be greater. Based on our results this was not, however, the case; instead, the reverse was true, especially in young and old age groups. The Finnish reference value of DL_{CO} was in all age groups 3–20% smaller than the respective ECSC reference value.

The method used to obtain the Finnish reference value for DL_{CO} was to restrict the inspiratory volume by 90% of the measured VC value. The measurement made with a restrictor was easy to perform and repeatable (18). However, the use of an inhalation restrictor explains the finding that the Finnish DL_{CO} reference values (15) were lower than the ECSC reference values (11,16). This theoretical assumption gets more support from the experiment where diffusing capacity was determined for 10 healthy subjects with both methods; the diffusing capacity results were significantly lower when measured with the Finnish method. The difference varies, however, as is seen in Figure 1, depending on age and gender. Although the number of subjects participating in this experiment on the use of an inspiration restrictor was small, it might be argued that the DL_{CO} of Finnish people living in northern Europe, partly in a circumpolar area, would not differ from that of middle Europeans. On the other hand, use

of an inhalation restrictor only minimally influenced the TLC value because in calculation of TLC the whole measured VC was used.

The American Thoracic Society (ATS) and the European Respiratory Society (ERS) joint recommendation in 2005 (19) states that when the goal of inspiratory volume during the diffusing capacity test is 100% of VC, usually an inspiratory volume of only 90% of VC is gained. Based on this, the Finnish method, developed in the 1980s, that uses an inhalation restrictor at a volume level of 90% of measured VC seems to be good and practical. This method has been used in the Finnish reference values for DL_{CO} (15).

Specific diffusing capacity (DL_{CO}/VA) is a variable formed when DL_{CO} is divided by alveolar volume. Alveolar volume (VA) is measured based on helium dilution in the held breath during the diffusing capacity test, and its volume is near the TLC value. The size of the thoracic cavity also influences the value of VA; the greater the VA value, the smaller the DL_{CO}/VA.

The reference equations used were different. Both the ECSC and Finnish reference values for DL_{CO} were calculated based on age and height. The ECSC reference values for TLC were calculated only according to height, whereas the Finnish reference values for TLC were in addition formed by weight and age. The ECSC reference value for DL_{CO}/VA was formed by age and height, the Finnish value by age, height and weight.

ECSC reference values have been formed from several European and some North American reference values for Caucasians (16), while the Finnish reference values have been measured from railway workers and employers genetically from different parts of Finland (15). Both reference values were collected for the most part in the mid-1970s, although the ECSC reference values include older material.

The Finnish reference values were used for all original inhabitants in Finland from along the southern coast to Lapland. No comparisons were conducted between Sami and Finnish people, for example, but the austere Lappish climate could be assumed to favour an increase in lung volume (1). Thus, theoretically, the Finnish reference values would be better suited for Sami people than for the ECSC ones.

International recommendations for ethnic correction of TLC reference value vary (1,11–13), but usually TLC and RV reference values are corrected similarly to the FVC reference value (14). In the praxis of our laboratory, the diffusing capacity test on non-Finnish subjects was measured by the ECSC method (inspired volume, Vin, 100% of VC), and the ECSC reference values were used to interpret both diffusing capacity and lung volume results. For Finns, the diffusing capacity test was conducted using an inhalation restrictor at a level of Vin of 90% of VC and the Finnish reference values were used.

In 2005, the ATS/ERS recommended that new reference values for lung function be obtained (20). Although the Finnish reference values for DL_{CO} (15) are methodologically of high quality, they are based on a rather small population, 296 males and 257 females. Moreover, age groups beyond 65 years are lacking, which is why in Finland new reference values will be collected. Until these new values are available, a correction based on ethnic and methodological differences will be included in assessment of the results of diffusing capacity tests.

REFERENCES

1. Cotes JE. Lung function throughout life: Determinants and reference values. In: Lung function. Assessment and application in medicine. Fifth Edition. Oxford: Blackwell Scientific Publications; 1993. p. 445–513.
2. Yang T-S, Peat J, Keena V, Donnelly P, Unger W, Woolcock A. A reveiw of the racial differences in the lung function of normal Caucasian, Chinese and Indian subjects. Eur Respir J 1991;4:872–880.
3. Quanjer Ph H, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R. J-C Yearnault. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society Eur Respir J Suppl 1993;16:5–40.
4. Donnelly PM, Yang T-S, Peat JK, Woolcock JA. What factors explain racial differences in lung volumes? Eur Respir J 1991;4:829–838.
5. Rossiter CE, Weill H. Ethnic difference in lung function: evidence for proportional differences. Int J Epidemiol 1974;3:55–61.
6. Frisancho AR. Functional adaptation of high altitude hypoxia. Science 1975;187:313–319.
7. Pesola GR, Sunmonu Y, Huggins G, Ford JG. Measured diffusion capacity versus prediction equation estimates in blacks without lung disease. Respiration 2004;71:848–892.
8. Neas LM, Schwarzt J. The determinants of pulmonary diffusing capacity in a national sample of U.S. adults. Am J Respir Crit Care Med 1996;153:656–664.
9. Miller GJ, Saunders MJ, Gin RJ et al. Lung function in healthy boys and girls in Jamaica in relation to ethnic composition, test exercise performance and habitual physical activity. Thorax 1977;32:486–496.
10. Cotes JE, Saunders MJ, Adan JER, Anderson HR, Hall AM. Lung function in coastal and highland New Guineans – comparison with Europeans. Thorax 1973;28: 320–330.
11. Cotes JE, Chinn DJ, Quanjer PhH, Roca J, Yernault J-C. Standardization of the measurement of transfer factor (Diffusing capacity). Eur Respir J Suppl 1993;16: 41–52.
12. American Thoracic Society. Single-breath carbon monoxide diffusing capacity (transfer factor). Recommendations for a standard technique – 1995 update. Am J Respir Crit Care Med. 1995;152:2185–21898.
13. American Thoracic Society. Lung function testing: Selection of reference values and interpretative strategies. Am Rev Respir Dis 1991;144:1202–1218.
14. Stocks J, Quanjer Ph H. Reference values for residual volume, functional residual capacity and total lung capacity. Eur Respir J 1995;8:492–506.
15. Viljanen AA, editor. In: Reference values for spirometric, pulmonary diffusing capacity and body plethysmographic studies. Scand J Clin Invest Suppl. 1982;159:1–50.
16. European Community for Steel and Coal. Summary equations of reference values. Quanjer Ph H (Ed.). Bull Europ Physiopath Resp 1983;19(Suppl 5):7–10.
17. Piirilä P, Lindqvist A, Rytilä P, Välimäki P, Sovijärvi ARA. Mitä viitearvoja tulisi käyttää Suomeen muuttaneiden ulkomaalaisten spirometriatuloksia arvioitaessa? Suomen Lääkärilehti 2001;44:4487–4492.
18. Sovijärvi ARA. Day-to-day variation of single-breath diffusing capacity and lung volumes in patients with chronic obstructive lung disease, diffuse interstitial lung disease and in healthy subjects. Am Rev Respis Dis 1986;133(4), part 2:Abstr. A 385.
19. Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, Burgos F, Casaburi R, Coates A, Enright P, Gustafsson P, Hankinson J, Jensen R, McKay R, Miller MR, Navajas D, Pedersen OF, Pellegrino R, Wanger J. Standardisation of lung function testing – Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur Respir J 2005;26(4):720–735.
20. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, Coates A, van der Grinten CPM, Gustafsson P, Hankinson J, Jensen R, Johnson DC, MacIntyre N, McKay R, Miller MR, Navajas D, Pedersen OF, Wanger J. Interpretative strategies for lung function tests. Series "ATS/ERS task force: standardisation of lung function testing." Eur Respir J 2005:26(5):948–968.

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