

Lung function in Canadian Inuit: a follow-up study

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To assess the impact of acculturation on lung function, the forced vital capacity (FVC) and the 1-second forced expiratory volume (FEV₁) of 341 Inuit at Igloolik, NWT were measured. The same observers had used the same equipment to test 196 subjects in 1970–71. Cross-sectional analysis suggested that, relative to the previous decade, younger subjects had larger lung volumes (with gains of about 10% in FVC and 5% in FEV₁), while the elderly had smaller volumes (with losses of about 22% in FVC and 25% in FEV₁). Longitudinal analysis confirmed an accelerating loss of lung function in the older subjects: from age 25 to 35 years men and women had a loss in FVC of 13 and 11 mL/yr respectively, whereas from age 45 to 55 years the corresponding figures were 70 and 38 mL/yr. Cigarette smoking had increased substantially among the Inuit over the decade: the proportion of males and females smoking rose from 64% to 81% and from 85% to 93% respectively. Daily cigarette consumption per smoker increased from 11.8 to 20.2 and from 7.4 to 12.0 among men and women respectively. Nevertheless, the main explanation for the shape of the ageing curve is the survival of a small cohort of elderly Inuit with advanced tuberculosis. With control of this disease future cohorts of the elderly will have better lung function.

Dans le dessein de connaître l'effet de l'acculturation sur la fonction pulmonaire, les auteurs ont déterminé chez 341 Inuit d'Igloolik (TN-O) la capacité vitale maximum (CVM) et le vol expiratoire maximum seconde (VEMS) et comparé les moyennes avec celles obtenues par les mêmes observateurs, utilisant les mêmes techniques, sur 196 sujets en 1970–71. En 10 ans le volume pulmonaire moyen avait augmenté chez les jeunes (hausse d'environ 10% de la CVM et de 5% du VEMS) mais diminué chez les personnes âgées (baisse d'environ 22% de la CVM et de 25% du VEMS). L'analyse longitudinale confirme une perte fonctionnelle qui va s'accroître avec l'âge: dans la CVM elle passe de 13 mL/an (de 25 à 35 ans) à 70 mL/an (de 45 à 55 ans) chez les hommes et de 11 à 38 mL/an chez les femmes aux mêmes âges. L'usage de la cigarette par les Inuit a fort augmenté pendant ces 10 ans, la proportion des fumeurs étant passée de 64% à 81% chez les hommes et de 85% à 93% chez les femmes; le nombre moyen de cigarettes par jour a augmenté de 11,8 à 20,2 chez les hommes et de 7,4 à 12,0 chez les femmes. Il reste que la raideur de la courbe

du vieillissement s'explique surtout par la survie d'un petit groupe d'Inuit âgés atteints de tuberculose à un stade avancé. Comme il est maintenant possible de surmonter cette maladie, les Inuit âgés de demain jouiront d'une meilleure fonction pulmonaire.

In 1970–71 we found that the forced vital capacity (FVC) and the 1-second forced expiratory volume (FEV₁) of Inuit living in the Igloolik region of the Canadian Arctic were both greater than predicted from age and standing height, despite frequent histories of tuberculosis and the prevalence of respiratory adenovirus infections.¹ Possible explanations included a high level of habitual physical activity, an unusual body build and limited exposure to cigarette smoke and air pollutants.

We repeated the testing 10 years later (1980–81). In the intervening period acculturation had been associated with a 10-fold increase in snowmobile ownership, gradual abandonment of traditional hunting and deterioration of cardiorespiratory fitness in all except boys aged 15 years or younger. Control of tuberculosis had become virtually complete,² while cigarette consumption had risen toward levels typical of "white" society. We examined the impact of these changes on pulmonary function, using both cross-sectional and longitudinal epidemiologic analysis.

Methods

Subjects

Volunteers were recruited from the Inuit settlement of Igloolik, NWT (69°40'N) in accordance with a protocol approved by the village council and the University of Toronto's Committee on Human Experimentation.

The population of the settlement had increased from 530 in 1970–71 to 719 in 1980–81. We tested 198 males and 143 females (75% and 60% of the male and female population aged 9 years and older respectively, compared with 73% and 64% in 1970–71³).

As in our previous study,¹ the subjects were subdivided into a group of "healthy" people (157 males and 98 females) and a group of people with a history of respiratory disease (41 males and 45 females) on the basis of records from the nursing station at Igloolik. The records showed that 33% of the population had a history of respiratory disease, compared with 25% of our subjects.

The community still formed a steep age pyramid in 1980–81: there were 39 men and 24 women aged 20 to 29 years, and 10 men and 7 women aged 50 to 59 years among our subjects. The average standing height of the men was 165.6 ± 5.4 cm at age 25 years and 161.4 ± 4.6 cm at age 55 years, while for the women the corresponding values were 154.5 ± 5.4 cm and 150.4 ± 4.0 cm respectively.

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Cigarette smoking

Information on smoking was obtained by interviewing the subjects. Since one of us (A.R.) had lived in the settlement and knew the habits of the subjects, we had confidence in the accuracy of this information.

Spirometry

A standard 13.5-L Stead-Wells spirometer was used. The subjects were seated and were allowed two practices, followed by three definitive trials. The reported results are means for the three definitive trials.

Results

Cigarette smoking

In the 1970-71 survey¹ 64% of males and 85% of females aged 14 years or older reported that they smoked cigarettes, with the average consumption being 11.8 ± 4.6 and 7.4 ± 3.0 cigarettes per day respectively. In 1980-81 81% of males and 93% of females described themselves as smokers, with consumption averaging 20.2 ± 9.1 and 12.0 ± 5.3 cigarettes per day respectively (increases of 71% and 81% respectively, $p < 0.001$).

Forced vital capacity

Cross-sectional comparison of the data for 1970-71 and 1980-81 showed a significant improvement in FVC among men aged 20 to 29 years but a significant worsening in the oldest group (Table I). The data for the female subjects showed a similar trend (Table I). However, if those with a history of respiratory disease are excluded the values for subjects 60 years or older are no lower than they were in 1970-71.

Longitudinal comparisons based on repeat testing of the same subjects showed initial values similar to those found with the cross-sectional technique, with a decrease in FVC (mean \pm standard error [SE]) of 13 ± 13 , 47 ± 6 and 70 ± 15 mL/yr for men aged 25 ($n =$

17), 35 ($n = 17$) and 45 ($n = 6$) years respectively in 1970-71. The corresponding values for women were 11 ± 6 , 23 ± 7 and 38 ± 9 mL/yr ($n = 13$, 11 and 5). Plainly the loss of lung capacity accelerated with age.

Forced expiratory volume

Again, cross-sectional comparison suggested some improvement in FEV₁ among the young adults but a worsening of FEV₁ among those aged 50 to 59 years (Table I). If those with a history of respiratory disease are excluded the values for the latter group are no lower than they were in 1970-71.

Longitudinal analysis showed a loss in FEV₁ (mean \pm SE) of 23 ± 9 , 42 ± 6 and 54 ± 8 mL/yr for men aged 25, 35 and 45 years respectively in 1970-71. The corresponding values for women were 3 ± 11 , 29 ± 7 and 36 ± 6 mL/yr. Like the loss of capacity, the loss of function accelerated with age.

Lung function in children and adolescents

The lung function in children and adolescents is best related to body size through logarithmic equations of the type $FVC = A + H^B$, where A is estimated body area, H is height and B is an arbitrary exponent. In 1980-81 all height exponents were greater than 3.00. The one exponent less than 3.00 in 1970-71 increased to 3.11 in 1980-81 (Table II).

Table II—Exponents relating lung volumes to height in Inuit children and adolescents (aged 9 to 19 years)

Exponent	Boys		Girls	
	1970-71 (n = 46)	1980-81 (n = 94)	1970-71 (n = 32)	1980-81 (n = 69)
Forced vital capacity to height	3.28	3.43	3.01	3.41
Forced expiratory volume to height	3.31	3.29	2.50	3.11

Table I—Results of testing of lung function in Inuit at Igloolik, NWT in 1970-71 and 1980-81

Sex and age group (yr)	Mean \pm standard deviation (and no. of subjects)			
	Forced vital capacity		1-second forced expiratory volume	
	1970-71	1980-81	1970-71	1980-81
Men				
20-29	5.12 ± 0.54 (30)	$5.41 \pm 0.62^\dagger$ (39)	4.03 ± 0.53 (30)	$4.44 \pm 0.46^*$ (39)
30-39	4.86 ± 0.61 (25)	4.90 ± 0.83 (31)	3.68 ± 0.59 (25)	3.73 ± 0.76 (31)
40-49	4.42 ± 0.83 (9)	4.54 ± 0.72 (18)	3.26 ± 0.74 (9)	3.40 ± 0.72 (18)
50-59	4.50 ± 0.43 (5)	$3.34 \pm 0.89^*$ (10)	3.41 ± 0.32 (5)	$2.39 \pm 0.88^*$ (10)
Women				
20-29	3.77 ± 0.46 (21)	4.02 ± 0.50 (24)	3.00 ± 0.47 (21)	$3.28 \pm 0.45^\dagger$ (24)
30-39	3.47 ± 0.53 (17)	3.83 ± 0.59 (24)	2.70 ± 0.50 (17)	3.04 ± 0.59 (24)
40-49	3.03 ± 0.21 (6)	3.38 ± 0.68 (15)	2.31 ± 0.21 (6)	2.56 ± 0.57 (15)
50-59	3.13 ± 0.45 (5)	$2.58 \pm 0.22^\dagger$ (7)	2.34 ± 0.47 (5)	1.84 ± 0.27 (7)

* $p < 0.01$.

† $p < 0.05$.

Specific diagnoses

Specific diagnoses were drawn from the nursing station records. All had been confirmed by radiography.

Although a history of respiratory disease had a substantial effect on the apparent rate of ageing, the average discrepancy between the results for this group of subjects and those with no history of respiratory disease was small. Expressed as a percentage of the values for the "healthy" Inuit of the same age and height, the FVC was $95.5\% \pm 2.4\%$ for males and $98.4\% \pm 2.6\%$ for females. The corresponding values for FEV_1 were $93.9\% \pm 3.0\%$ and $99.0\% \pm 2.9\%$ respectively.

Most of the subjects with a history of respiratory disease (32 of the 41 men and 27 of the 45 women) had been ascribed diagnoses of primary tuberculosis, hilar calcification or primary tuberculosis with hilar calcification; such radiographic findings had little apparent effect on lung function. Seven men and 11 women had pulmonary fibrosis, and in the men this appreciably reduced the FEV_1 . Two men and seven women had combinations of advanced tuberculosis with fibrosis, bronchiectasis or emphysema. Their respiratory function was sufficiently impaired to limit oxygen transport (the predicted maximum oxygen intake was 81% of normal for eight of the nine who were able to perform a step test). Seven of these subjects were over the age of 40 years.

Discussion

Cigarette smoking

As in other developing societies, there has been a substantial increase in cigarette consumption among the Inuit over the past decade, and ever-younger people are smoking cigarettes regularly. Nevertheless, there is no clear indication that lung function in the Inuit has deteriorated over the past decade. This is likely because the harmful effects of cigarette smoking take 20 to 30 years to become apparent. It is also possible that changes in cigarette design or smoking patterns or both⁴ have resulted in a relatively constant exposure to tar and nicotine despite increased cigarette purchases. A further possible factor is that the respiratory handicaps of their traditional way of life (i.e., tuberculosis, exposure to cold and domestic air pollution) have now been replaced by a cigarette handicap.

Secular trends of lung function

The gains in lung function in the young adults might be attributable to an increase in stature of the population, since many observers, including ourselves,¹ have shown that lung volumes increase approximately as the cube of the height. Although the young adults were no taller than those examined 10 years previously, we suspect that trauma to the vertebral column from snowmobiling is masking a secular trend of an increase in stature (unpublished observations, 1984). The gains may also be due to better rapport with the subjects, the virtual elimination of tuberculosis^{2,5} and avoidance of the rigours of nomadic hunting (e.g., inhalation of Arctic

air by day and the polluted air of the igloo by night⁶).

The poor average lung volumes in the oldest adults seem due mainly to their being a small cohort with histories of secondary tuberculosis. When this group is excluded from the sample the rate of change in this index of ageing has not increased. Both cross-sectional and longitudinal statistics for the community are heavily influenced by this cohort effect. Presumably, lesser social supports and the absence of effective treatment for tuberculosis caused death at a much earlier age in previous decades.²

Effects of respiratory disease

The changes in respiratory function resulting from advanced tuberculosis were associated with a substantial decrease in predicted maximum oxygen intake, although in healthy subjects pulmonary ventilation has only a minor influence on maximum oxygen transport.⁷ Destruction of pulmonary tissue could conceivably increase the heart rate response to a given intensity of submaximal effort, partly because of sensations arising in the fibrosed lung tissue and partly because of destruction of the pulmonary vascular bed. It is also quite likely that those with a history of severe disease were physically less active and thus failed to realize their oxygen transport potential.

Regional comparisons

Schaefer and colleagues⁶ collected data for male Inuit living at Arctic Bay. The average height of their subjects was very similar to that of our subjects (e.g., 165.9 ± 3.8 cm at 20 to 24 years v. 165.4 ± 5.6 cm at 25 years). Lung function values for young adults were also very similar, but the apparent rate of ageing (as gauged from cross-sectional data) was much greater at Arctic Bay than at Igloolik. It is unlikely that either the larger proportion of miners at Arctic Bay or the extent of pneumoconiosis among them is sufficient to explain this discrepancy.⁶ Nor do we believe there is an intrinsically greater risk of cold-induced lung damage⁶ at Arctic Bay. The hunters of this settlement must travel further than those of Igloolik when seeking caribou, and this increases the duration of exposure to cold, but the more northerly latitude of Arctic Bay does not give a materially harsher climate. The most reasonable explanation seems to be that already adduced to explain the findings at Igloolik: a differing incidence of respiratory disease at the various settlements,^{6,8} together with selective sampling of fit individuals by the physiologists and of respiratory disease by the visiting medical specialists.³

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Adjuvant BCG immunotherapy for malignant melanoma

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A total of 199 patients with stage I malignant melanoma at Clark's level 3 to 5 of invasion were entered into a prospectively controlled randomized clinical trial that attempted to assess the value of local and systemic immunotherapy with BCG (bacille Calmette-Guérin) after surgery. The patients were randomly assigned, with stratification by Clark's level, to receive either routine follow-up or immunotherapy with BCG, administered intradermally with a Heaf gun around the site of wide excision and then given orally for 2 years. Intradermal administration of BCG was repeated after 1 year's oral therapy with BCG. Of the 99 patients in the treatment group 66 had Clark's level 3, 28 had level 4, and 5 had level 5 invasion. Of the 100 patients in the control group, 61 had level 3, 36 had level 4, and 3 had level 5 invasion. Other prognostic factors, such as sex, depth of invasion, histologic features, site of disease and type of surgery, were evenly distributed.

There were 57 recurrences of the melanoma, 24 in the treatment group and 33 in the control group. However, this trend was not statistically significant ($p = 0.194$). The suggestion that BCG may reduce the likelihood of local/regional recurrence has not been confirmed with longer follow-up. There were 13 such recurrences in the BCG group, compared with 21 in the control group; the proportions of patients in each group who had such a recurrence were not significantly different. Of the 199 patients 41 died, 24 in the control group and 17 in the treatment group; again, this difference was not significant. While there may be minor activity in selected patients, there appeared to be no benefit from this form

of adjuvant BCG therapy in patients with malignant melanoma.

Un total de 199 patients souffrant de mélanome malin au stade I ayant un niveau d'invasion entre 3 et 5 selon la classification de Clark ont servi de sujets pour une étude clinique randomisée contrôlée prospectivement. Cette étude avait pour but d'évaluer la valeur de l'immunothérapie systémique ou locale au BCG (bacille Calmette-Guérin) après la chirurgie. Les malades ont été placés au hasard dans deux groupes stratifiés selon le niveau d'invasion de la classification de Clark. Un premier groupe devait être simplement suivi; le deuxième groupe recevait une immunothérapie au BCG administré de façon intradermique avec un inoculateur Heaf autour l'endroit de la grande excision, et puis administré oralement pendant 2 ans. L'administration intradermique du BCG était répétée après 1 an de traitement oral. Des 99 patients traités, 66 étaient au niveau 3 de Clark, 28 étaient au niveau 4, et 5 étaient au niveau 5. Des 100 patients non traités, 61 étaient au niveau 3, 36 étaient au niveau 4, et 3 étaient au niveau 5. La répartition dans les deux groupes d'autres facteurs pronostiques, tels le sexe, la profondeur de l'invasion, l'histologie, le siège de la maladie et le type de chirurgie, était semblable.

Il y a eu 57 cas de récurrence du mélanome malin, dont 24 dans le groupe traité et 33 dans le groupe témoin. Néanmoins, cette différence n'était pas statistiquement significative ($p = 0,194$). La possibilité que le BCG puisse réduire les récurrences locales ou régionales n'a pas été confirmée par un plus long suivi. Treize récurrences de ce type se sont produites dans le groupe traité et 21 dans le groupe témoin; la proportion de malades subissant cette récurrence ne différait pas de façon significative d'un groupe à l'autre. Des 199 patients, 41 sont morts, 24 du groupe témoin et 17 du groupe traité; là encore, la différence n'était pas significative. Si une certaine activité mineure due au BCG peut être constatée chez certains malades, l'utilisation d'une immunothérapie adjuvante au BCG chez des malades atteints de mélanome malin ne semblait pas avoir d'avantages.

Observation of the natural history of malignant melanoma has been an important stimulus to the clinical evaluation of immunotherapy in this disease. Well

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