EPIDEMIOLOGY

Serum carotenoids, vitamins A and E, and 8 year lung function decline in a general population

A Guenégué, B Leynaert, I Pin, G Le Moël, M Zureik, F Neukirch

Background: Oxidative stress is thought to have a major role in the pathogenesis of airway obstruction. A study was undertaken to determine whether subjects with low levels of antioxidants (serum β-carotene, α-carotene, vitamins A and E) would be at a higher risk of accelerated decline in forced expiratory volume in 1 second (FEV₁) as their lungs would be less protected against oxidative stress.

Methods: 1194 French subjects aged 20–44 years were examined in 1992 as part of the European Community Respiratory Health Survey (ECRHS); 864 were followed up in 2000 and 535 (50% men, 40% lifelong non-smokers) had complete data for analysis.

Results: During the 8 year study period the mean annual decrease in FEV₁ (adjusted for sex, centre, baseline FEV₁, age, smoking, body mass index and low density lipoprotein cholesterol) was 29.8 ml/year. The rate of decrease was lower for the subjects in tertile I of β-carotene at baseline than for those in the other two tertiles (−36.5 v. −27.6 ml/year; p = 0.004). An increase in β-carotene in the two surveys was associated with a slower decline in FEV₁. No association was observed between α-carotene, vitamin A, or vitamin E and FEV₁ decline. However, being a heavy smoker (>20 cigarettes/day) in combination with a low level of β-carotene or vitamin E was associated with the steepest decline in FEV₁ (−52.5 ml/year, p = 0.0002 and −50.1 ml/year, p = 0.010, respectively).

Conclusions: These results strongly suggest that β-carotene protects against the decline in FEV₁ over an 8 year period in the general population, and that β-carotene and vitamin E are protective in heavy smokers.
respectively, which is comparable to that found in the study.

In bivariate analyses, the relationships between anti-

higher risk of accelerated FEV1 decline), we classified serum

protected against oxidative stress and they would thus be at

the higher tertiles (tertiles II and III) with those in

antioxidant levels into tertiles and compared subjects with

m in antioxidant concentration (in

differences between the tertiles, all estimated by analysis of

variance).

The effect of changes in antioxidant levels on lung function

was analysed by including the mean annual change

was expressed in ml/year (value at

baseline, p < 0.0001). The vitamin A concentration was

negatively correlated with both

β-carotene and α-carotene concentrations in

1992 were positively correlated with each other (r = 0.073, p = 0.011). The associations of both antioxidant levels and

FEV1, age, BMI, and LDL cholesterol were taken into account. Confounding factors were sex and

baseline values of FEV1, age, BMI, and LDL cholesterol

were introduced as quantitative variables. We paid special

attention to tobacco smoking, a major risk factor for FEV1

decline, which may be an effect modifier as well as a

confounder. Baseline smoking status was classified into four

categories: never-smokers, ex-smokers (stopped for

≥ 1 year), moderate smokers (< 20 cigarettes/day), and heavy

smokers (≥ 20 cigarettes/day). In the analyses of the

interactions between antioxidant levels and smoking, we

coded baseline smoking status as heavy smoking compared

with any other status. Smoking between the two time points

was assessed as either pack years (product of the number of

cigarettes smoked per day and the number of years of smoking)

or as the change in smoking status (start or increase, retain, and

Table 1 Characteristics of study participants (n = 535, 50% men)*

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>36.9 (7.1)</td>
<td>45.2 (7.1)</td>
</tr>
<tr>
<td>Smoking status (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smokers</td>
<td>41.9</td>
<td>40.0</td>
</tr>
<tr>
<td>Former smokers</td>
<td>25.6</td>
<td>30.4</td>
</tr>
<tr>
<td>Moderate smokers (&lt;20 cigs/day)</td>
<td>20.8</td>
<td>19.9</td>
</tr>
<tr>
<td>Heavy smokers (&gt;20 cigs/day)</td>
<td>11.8</td>
<td>9.6</td>
</tr>
<tr>
<td>BMI (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight (≤ 20 kg/m²)</td>
<td>16.4</td>
<td>10.8</td>
</tr>
<tr>
<td>Normal (20–24.9 kg/m²)</td>
<td>63.9</td>
<td>56.8</td>
</tr>
<tr>
<td>Overweight (&gt;25–29.9 kg/m²)</td>
<td>17.6</td>
<td>25.8</td>
</tr>
<tr>
<td>Obese (&gt;30 kg/m²)</td>
<td>2.1</td>
<td>6.6</td>
</tr>
<tr>
<td>Current asthma (%)†</td>
<td>5.6</td>
<td>6.4</td>
</tr>
<tr>
<td>Chronic cough (%)‡</td>
<td>7.5</td>
<td>5.1</td>
</tr>
<tr>
<td>Chronic sputum (%)§</td>
<td>4.5</td>
<td>5.2</td>
</tr>
<tr>
<td>FEV1 (l/s)</td>
<td>3.67 (0.82)</td>
<td>3.42 (0.79)</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>102.3 (13.5)</td>
<td>104.9 (14.3)</td>
</tr>
<tr>
<td>FEV1/FVC &lt;70% (%)</td>
<td>4.3</td>
<td>5.2</td>
</tr>
<tr>
<td>Serum β-carotene (μmol/l)</td>
<td>0.40 (0.31)</td>
<td>0.64 (0.48)</td>
</tr>
<tr>
<td>Serum α-carotene (μmol/l)</td>
<td>0.096 (0.10)</td>
<td>0.13 (0.11)</td>
</tr>
<tr>
<td>Serum vitamin A (μmol/l)</td>
<td>1.91 (0.53)</td>
<td>2.02 (0.56)</td>
</tr>
<tr>
<td>Serum vitamin E (μmol/l)</td>
<td>23.0 (7.2)</td>
<td>29.0 (7.6)</td>
</tr>
<tr>
<td>Serum LDL cholesterol (g/l)</td>
<td>1.33 (0.40)</td>
<td>1.32 (0.36)</td>
</tr>
</tbody>
</table>

*BMI, body mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; LDL, low density lipoprotein.

*Quantitative variables are mean (SD).

†Subjects who answered “yes” to at least one of the two questions: “Have you had an attack of asthma in the last 12 months?” and “Are you currently taking any medicine including inhalers, aerosols or tablets for asthma?”

‡Subjects who answered “yes” to the two questions: “Do you usually bring up any phlegm from your chest during the day, or at night, in the winter?” and “Do you cough like this on most days for as much as three months each year?”

§Subjects who answered “yes” to the two questions: “Do you usually bring up any phlegm from your chest during the day, or at night, in the winter?” and “Do you bring up phlegm like this on most days for as much as three months each year?”

RESULTS

Characteristics of the study population and associations between antioxidants

The characteristics of the study population are shown in

Table 1. Half the participants were male. The mean (SD) age at

baseline (1992) was 36.9 (7.1) years. As expected in this

population of young adults, FEV1 values were in the normal

range.

As expected, β-carotene and α-carotene concentrations in

1992 were positively correlated with each other (r = 0.76 at

baseline, p < 0.0001). The vitamin A concentration was

negatively correlated with both β-carotene and α-carotene

recruited in Paris and Grenoble, subjects from the two

centres were analysed together. Nevertheless, the centre was

taken into account. Confounding factors were sex and

baseline values of FEV1, age, BMI, and LDL cholesterol

were introduced as quantitative variables. We paid special

attention to tobacco smoking, a major risk factor for FEV1

decline, which may be an effect modifier as well as a

confounder. Baseline smoking status was classified into four

categories: never-smokers, ex-smokers (stopped for

≥ 1 year), moderate smokers (< 20 cigarettes/day), and heavy

smokers (≥ 20 cigarettes/day). In the analyses of the

interactions between antioxidant levels and smoking, we

coded baseline smoking status as heavy smoking compared

with any other status. Smoking between the two time points

was assessed as either pack years (product of the number of

packs smoked per day and the number of years of smoking)

or as the change in smoking status (start or increase, retain, and

stop or cut down).
Table 2  Factors associated with mean annual decline in FEV\textsubscript{1} (crude associations)

<table>
<thead>
<tr>
<th>Variables (baseline values)</th>
<th>Mean (SD) FEV\textsubscript{1} decline (ml/year)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
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</tr>
<tr>
<td>Male</td>
<td>-34.2 (35.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>-25.5 (27.5)</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>-22.2 (26.4)</td>
<td>0.007</td>
</tr>
<tr>
<td>26–30</td>
<td>-20.8 (28.9)</td>
<td></td>
</tr>
<tr>
<td>31–35</td>
<td>-29.4 (26.2)</td>
<td></td>
</tr>
<tr>
<td>36–40</td>
<td>-32.1 (30.1)</td>
<td></td>
</tr>
<tr>
<td>&gt;40</td>
<td>-33.6 (36.1)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>-29.7 (30.1)</td>
<td>0.16</td>
</tr>
<tr>
<td>Former</td>
<td>-28.5 (31.0)</td>
<td></td>
</tr>
<tr>
<td>Moderate (&lt;20 cigs/day)</td>
<td>-27.2 (22.5)</td>
<td></td>
</tr>
<tr>
<td>Heavy (&gt;20 cigs/day)</td>
<td>-37.9 (46.2)</td>
<td></td>
</tr>
<tr>
<td>FEV\textsubscript{1} (l/l)</td>
<td></td>
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<tr>
<td>1st tertile</td>
<td>-21.8 (34.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2nd tertile</td>
<td>-30.1 (28.9)</td>
<td></td>
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<tr>
<td>3rd tertile</td>
<td>-37.6 (30.1)</td>
<td></td>
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<tr>
<td>BMI (kg/m\textsuperscript{2})</td>
<td></td>
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</tr>
<tr>
<td>Underweight (&lt;20)</td>
<td>-23.6 (35.0)</td>
<td>0.004</td>
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<tr>
<td>Normal (20–24.9)</td>
<td>-29.7 (28.6)</td>
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</tr>
<tr>
<td>Overweight (25–29.9)</td>
<td>-34.3 (38.9)</td>
<td></td>
</tr>
<tr>
<td>Obese (&gt;30)</td>
<td>-46.9 (27.7)</td>
<td></td>
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<tr>
<td>LDL cholesterol (g/l)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st tertile</td>
<td>-24.3 (31.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>2nd tertile</td>
<td>-31.8 (32.2)</td>
<td></td>
</tr>
<tr>
<td>3rd tertile</td>
<td>-32.4 (32.0)</td>
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*Heavy smokers vs any other status (p for comparison = 0.045).
†Tertile limits for FEV\textsubscript{1}: 1.60–3.125, 3.125–4.025, 4.025–6.02 l/s.
‡Tertile limits for LDL cholesterol concentration: 1.12–1.875, 1.875–2.295, 2.295–3.94 g/l.

Factors associated with lung function decline

The crude mean annual decline in FEV\textsubscript{1} according to sex and age, smoking status, FEV\textsubscript{1}, BMI, and serum level of LDL cholesterol in 1992 are shown in table 2. The decline in FEV\textsubscript{1} was significantly steeper in men than in women, and was positively associated with baseline FEV\textsubscript{1}, age, BMI, and LDL cholesterol levels. Socioeconomic status (age at completion of full time education), physical activity (exercise resulting in breathlessness or sweating more than once a week), and occupational exposure (having worked in a job in which there was exposure to vapours, gas, dust or fumes) were not associated with lung function decline.

Association between lung function decline and antioxidant concentrations at baseline

After adjustment for potential confounding factors, only \( \beta \)-carotene concentration was associated with the decline in FEV\textsubscript{1} and subjects in tertiles II and III had a very similar FEV\textsubscript{1} decline (table 3). FEV\textsubscript{1} declined significantly faster in subjects in tertile I of \( \beta \)-carotene concentration (−36.5 ml/year (95% CI −41.5 to −31.6)) than subjects pooled from tertiles II and III (−27.6 ml/year (95% CI 31.2 to −23.9), p = 0.004), which corresponds to a supplemental FEV\textsubscript{1} decline of 9.0 ml/year on average (95% CI 2.9 to 15.1) for subjects in tertile I compared with subjects in tertiles II and III combined. Similar results were observed after excluding subjects with either current asthma (p = 0.024) or FEV\textsubscript{1}/FVC <70% (p = 0.06). The results did not change when baseline smoking status was replaced by the number of pack years between the two time points (FEV\textsubscript{1} decline: −35.2 ml/year (95% CI −40.2 to −30.1) in tertile I v −26.7 ml/year (95% CI −29.9 to −23.4) in tertiles II and III combined, p = 0.007) or when the change in smoking status was added to the model (FEV\textsubscript{1} decline: −35.3 ml/year (95% CI −41.2 to −29.3) in tertile I v −26.8 ml/year (95% CI −31.7 to −21.9) in tertiles II and III combined, p = 0.007). The interaction term between sex and tertiles of \( \beta \)-carotene was not significant (p = 0.28).

When all antioxidants were included simultaneously in the same regression model, \( \beta \)-carotene remained significantly and independently associated with decline in lung function. The mean annual decline in FEV\textsubscript{1} was −37.7 ml/year (95% CI −43.0 to −32.4) in tertile I v −25.2 ml/year (95% CI −29.6 to −20.8) in tertiles II and III combined (p = 0.0005).

Interaction between baseline low levels of antioxidants and heavy smoking

We explored the potential modification of the association between \( \beta \)-carotene and FEV\textsubscript{1} decline by tobacco smoking. We first analysed lifelong non-smokers separately to discard any possible residual confounding by tobacco. The FEV\textsubscript{1} of subjects in tertile I of \( \beta \)-carotene declined −37.8 ml/year (95% CI −46.1 to −21.9) whereas that of the subjects in tertiles II and III combined declined −25.6 ml/year (95% CI −30.0 to −21.0) (p = 0.013). We next analysed the effects of the interaction between heavy smoking and a low antioxidant level on FEV\textsubscript{1} decline. We found that FEV\textsubscript{1} declined at a rate of −52.5 ml/year (95% CI −64.4 to −40.6) (p for interaction = 0.031) in subjects who were heavy smokers in 1992 and had a low \( \beta \)-carotene level (tertile I) in 1992 (fig 2). The interaction with vitamin E was also significant (p = 0.042): FEV\textsubscript{1} declined at a mean rate of −50.1 ml/year (95% CI −65.2 to −35.0) in heavy smokers with low vitamin E levels. Interactions with \( \alpha \)-carotene and vitamin A were not significant.
Association between lung function decline and changes in levels of antioxidants between 1992 and 2000

We first assessed FEV\textsubscript{1} decline according to the tertiles of \(\beta\)-carotene concentration in 1992 and 2000 (table 4). The subjects in tertile I at both time points had the steepest decline in FEV\textsubscript{1} (−40.0 ml/year) whereas those in tertile II or III at both time points had the slowest decline (−26.7 ml/year).

We next analysed the association between the decline in FEV\textsubscript{1} and changes in antioxidant levels treated as continuous variables (mean annual changes). In the whole study population, an increase in \(\beta\)-carotene of 0.5 µmol/l (corresponding to 1 SD of change in \(\beta\)-carotene level per year\textsuperscript{10} years) reduced the decline in FEV\textsubscript{1} by 25.5 ml (\(p = 0.048\)) over 10 years, which approximately counteracts the effect of 4 years of ageing.

Figure 2. Adjusted* mean (95% CI) annual decline in FEV\textsubscript{1} (ml/year) according to antioxidant levels (tertile I v tertiles II and III combined) and heavy smoking (heavy smokers v others) at baseline (ECRHS I, 1992). *Multiple linear regression including sex, centre and baseline data for FEV\textsubscript{1}, age, BMI, and LDL cholesterol.

FIGURE 1

DISCUSSION

This is the first longitudinal study to explore the relationships between decline in lung function and serum levels of \(\beta\)-carotene, \(\alpha\)-carotene, vitamin A, and vitamin E. Serum levels are likely to be better markers of lung tissue concentrations than dietary intakes assessed by questionnaires.\textsuperscript{1,2} We found that the \(\beta\)-carotene concentration was independently associated with the decline in FEV\textsubscript{1}, with the steepest decline occurring in subjects with the lowest \(\beta\)-carotene levels at baseline. No such association was observed for \(\alpha\)-carotene, vitamin A, or vitamin E concentrations. However, being a
heavy smoker with a low level of β-carotene or vitamin E was associated with the stepepest FEV 1 decline. An increase in β-carotene concentration between the two surveys was associated with a slower decline in FEV 1. These results strongly suggest that β-carotene protects lung function in the general population and that β-carotene and also vitamin E have a protective effect in heavy smokers.

**Validity and possible limitations**

The protocol of the ECRHS was highly standardised and the quality of data was strictly controlled. As in any longitudinal study, there was some loss to follow up. However, our response rate is comparable to a recent population study. Not having all data available for all subjects may have affected representativeness. The subjects who were analysed were less than 2 years older than those excluded. Such a small difference is unlikely to have biased the association between lung function decline and antioxidants due to the young age of the study population and the small range of values (20–4 years in 1992). Analysed subjects were more frequently non-smokers and less frequently heavy smokers. This can only have weakened the overall association between antioxidants and lung function decline, as the association was stronger in heavy smokers. Participants had also less frequently worked in jobs where they were exposed to vapours, dust, gas or fumes than excluded subjects. If antioxidants act against occupational noxious particles as against cigarette smoke, the possible bias would be the same as for smoking habits. Mean age at full time education in the analysed subjects was slightly higher than in the excluded subjects. This could mean that the analysed subjects had a more affluent lifestyle and thus a higher intake of anti-oxidants. Levels of β-carotene were similar to those described in a study comparing five European countries including France.

**Consistency of the findings**

The relationships between FEV 1 decline and serum levels of β-carotene and α-carotene have never been explored, so we cannot compare our results with other studies. However, the internal consistency of the results is supported by the fact that the results were identical in the whole study population. However, we found that the antioxidant values (20–2 years) at baseline were only moderately correlated (r = 0.27, p = 0.0001), we simultaneously included both serum LDL cholesterol levels and BMI in the models. Other demographic and lifestyle factors such as educational level, physical activity, and occupational exposure are potential confounders but were not associated with FEV 1 decline in our study, and adjusting for these factors did not change the results (data not shown).

Levels of β-carotene, vitamin A, and vitamin E were similar to those reported in studies exploring cross sectional relationships between lung function and serum levels of antioxidants. Levels of α-carotene were similar to those described in a study comparing five European countries including France.

<table>
<thead>
<tr>
<th>Tertiles of antioxidants in 1992</th>
<th>I</th>
<th>II-III</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=95</td>
<td>40.0 (46.3 to 33.7)†</td>
<td>29.0 (36.3 to 21.5)</td>
</tr>
<tr>
<td>n=66</td>
<td>31.5 (39.0 to 23.9)</td>
<td>26.7 (30.8 to 22.6)†</td>
</tr>
<tr>
<td>n=286</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Multiple linear regression including sex, centre, and baseline values of FEV 1, age, smoking status, BMI, and LDL cholesterol. tp = 0.004, tertile I at both time points v the others.

Table 4: Mean (95% CI) adjusted* annual FEV 1 decline (ml/year) according to tertiles of β-carotene in 1992 and in 2000.

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been shown that β-carotene and vitamin E are transported by LDL lipoproteins. To our knowledge, the association between lung function and LDL cholesterol has been investigated in only one study using the data from the Third National Health and Nutrition Examination Survey. The results were only cross sectional. Of the 14 135 subjects analysed (≥ 17 years), LDL levels were negatively associated with FEV 1 despite adjustment for BMI, and the association was strengthened after further adjustment for serum antioxidants (vitamin E, β-carotene, vitamin C, selenium). These results may be explained by the oxidation of LDL contributing to endogenous oxidative stress. As BMI and LDL levels at baseline were only moderately correlated (r = 0.27, p < 0.0001), we simultaneously included both serum LDL cholesterol levels and BMI in the models. Other demographic and lifestyle factors such as educational level, physical activity, and occupational exposure are potential confounders but were not associated with FEV 1 decline in our study, and adjusting for these factors did not change the results (data not shown).

The relationships between FEV 1 decline and serum levels of β-carotene and α-carotene have never been explored, so we cannot compare our results with other studies. However, the internal consistency of the results is supported by the fact that the results were identical in the whole study population, in lifelong non-smokers, and when regression models were adjusted for baseline smoking status, baseline smoking status plus change in smoking status, or cumulative exposure assessed by pack years. Our results are also consistent with the results from observational studies on lung cancer risk. However, interventional trials of β-carotene supplementation showed an unexpected negative effect or no beneficial effect on the risk of lung cancer. A biologically plausible explanation for these unlikely findings has yet to be found.

Vitamin A and vitamin E have already been analysed in longitudinal studies, with data collected using dietary questionnaires. One study that followed 1346 adults aged 18–70 years for 9 years found no association between the decline in FEV 1 and intakes of either vitamin A or vitamin E, even in interaction with smoking status (coded as never smokers, 1 month ex-smokers, and current smokers). In another study in which 2512 men aged 45–59 years were followed for 5 years, neither average intake nor change in vitamin E intake was found to be related to change in lung function. Our results are consistent with the findings of these two studies: we found no association between vitamin A or vitamin E concentrations and lung function decline in the whole study population. However, we found that the interaction between low levels of vitamin E and heavy smoking had a strong effect on lung function decline.

Two hypotheses have been proposed to explain the effect of smoking status: (1) some antioxidants may neutralise "general" oxidants (those naturally encountered by non-smokers) more efficiently than oxidants found in cigarettes; and (2) some antioxidants may be more efficient when the oxidative stress is high. Our results agree with both hypotheses to some extent. Firstly, we observed that in non-smokers (with normal oxidative stress) high levels of β-carotene were associated with a less rapid decline in FEV 1, which suggests that β-carotene is able to scavenge environmental or endogenous oxidants. Secondly, when the...
oxidative stress increased, as is the case in heavy smokers. Low levels of β-carotene and also of vitamin E were associated with a more rapid decline in FEV₁ (exceeding −50 ml/year). These antioxidants therefore seem to be able to partly counteract the damage caused by oxidants associated with heavy smoking, because the mean rate of FEV₁ decline in heavy smokers with high levels of antioxidants was similar to that in other subjects. The hypothesis of a threshold effect of oxidative stress may explain why antioxidant levels did not interact with smoking in general when moderate and heavy smokers were pooled together versus the other smoking status (data not shown). In fact, the oxidant burden due to tobacco smoking in moderate smokers may have been too low. In our study sample the amount of tobacco smoked by heavy smokers was much greater than that smoked by moderate smokers with mean (SD) pack years at baseline in heavy smokers almost three times higher than in moderate smokers (29.0 (14.5) v 10.0 (8.9) pack years, p = 0.0001). Moreover, heavy smokers started smoking at a younger age than moderate smokers (16.8 (2.6) v 18.6 (4.6) years, p = 0.002).

The results for heavy smokers should be discussed further. Heavy smokers were more sensitive to low levels of antioxidants than other subjects and also had lower mean β-carotene levels. This lower level may be due to lower dietary intakes or to metabolic differences resulting in lower serum concentrations of β-carotene at similar dietary intakes to non-smokers. In some studies, smokers have been shown to have significantly lower dietary antioxidant intake than non-smokers. In a large study of 1483 subjects aged 16–64 years it was found that, for the same level of dietary intake, smokers were more likely to have lower circulating levels of β-carotene than non-smokers. Another study showed an increase in the plasma concentration of β-carotene, α-carotene, and vitamins A and E in 15 smokers after 4 weeks of smoking cessation. Nevertheless, as the strength of the correlation coefficients between serum antioxidant levels and dietary antioxidant intake was only moderate, we cannot exclude a possible genetic influence or gene–environment interaction in the relationships between lung function decline, smoking, and antioxidant levels.

Possible mechanisms for the associations between antioxidants and lung function decline

There may be at least two explanations for the association between lung function decline and β-carotene and vitamin E concentrations. The first is antioxidant storage in the lungs. Redlich and co-workers examined the relationships between serum and lung tissue levels of β-carotene, α-carotene, vitamin A and vitamin E in 21 subjects undergoing a lung biopsy and found that serum and lung tissue levels of β-carotene were highly correlated (r = 0.72, p > 0.0001). Thus, in the case of attack by oxidants, β-carotene may come into direct contact with harmful molecules. Serum and lung tissue levels of vitamin E were also positively correlated, but not as strongly as for β-carotene (r = 0.47, p = 0.03). As we observed a correlation between lung function decline and vitamin E concentration only in heavy smokers, we suggest that vitamin E breaks the lipid peroxidation chain reaction only when oxidative stress increases. Redlich et al found that lung tissue levels of vitamin A were very low and did not correlate with serum levels. The lack of an association between the decline in FEV₁ and α-carotene levels may be explained by the low level of α-carotene in the lung tissue. Moreover, α-carotene and β-carotene levels are strongly associated in the serum (in our study as in a previous study) but not in the lung.

The second possible explanation is the specificity of the oxidants converted by β-carotene and vitamin E to a less reactive form. These two molecules scavenge the superoxide anion (O₂−) which can be shown positively to modulate airway smooth muscle contractility and proliferation. β-carotene and vitamin E may therefore protect against excessive airway smooth muscle contractility and/or proliferation by neutralising O₂− and thus protect against accelerated lung function decline.

In conclusion, this is the first longitudinal study to show that β-carotene and vitamin E may protect against accelerated decline in lung function, especially in heavy smokers. The decline in FEV₁ was twice as great in heavy smokers with low levels of β-carotene or vitamin E as in the general young adult population studied. Subjects who sustain heavy smoking and continue to have low antioxidant levels are probably at very high risk of developing chronic obstructive pulmonary disease (COPD). These powerful antioxidants may help to reduce oxidative stress—one of the factors thought to be involved in the pathogenesis of COPD—and thus may contribute to reducing the risk of morbidity and mortality related to this disease.

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