Some Short-term Effects of Changing to Lower Yield Cigarettes*

Barbara D. Minty, M.I.Biol; David Royston, FFARCS; and J. Gareth Jones, M.D.

The rate of clearance from the lung of the hydrophilic tracer molecule $^{99m}$Tc DTPA was used to investigate the short-term effects on lung epithelial function when smokers switched to cigarettes with lower yields of tobacco smoke constituents. Two separate studies were performed. In the first study, subjects smoked conventional mid- and low-tar cigarettes. The second study used two specially manufactured cigarettes with similar tar and nicotine yields, but differing carbon monoxide yields. Neither study demonstrated any significant improvement in $^{99m}$Tc DTPA clearance. The yields of carbon monoxide determined under standard machine smoking conditions implied that there would be a 44 percent reduction in exposure to carbon monoxide when subjects switched from smoking conventional mid-tar to low-tar cigarettes. However, measurements of carboxyhemoglobin showed that the smokers compensated for the lower yields and their exposure was reduced by only 11 percent. Similarly, in the second study, the subjects reduced their exposure by 7 percent instead of the expected 44 percent. Urine nicotine/ cotinine excretion measurements in this study indicated that there was no complimentary increase in nicotine absorption suggesting the possibility that subjects may be able to regulate their intake of individual components of the cigarette smoke. Thus, the unexpected result from this study was the finding that cigarette smokers could, in some way, regulate their intake of smoke from cigarettes of different composition so as to maintain a constant exposure of smoke constituents.

The lung is a major target organ for smoking-related disease. Because of the risk of lung disease, smokers have been recommended to give up the habit, or failing that, to change to cigarettes with lower yields of tar, nicotine and carbon monoxide.1,2

While there is evidence that cessation of smoking results in a slow improvement in abnormal pulmonary function, we are unaware of any evidence of improvement in pulmonary function test results when smokers change to lower yield cigarettes. However, a difficulty with this type of study arises from the long time course required for improvement in conventional tests of lung function even after complete cessation of smoking.3

A sensitive measure of a smoking-related abnormality in lung function is the increased rate of clearance of the hydrophilic tracer molecule $^{99m}$Tc diethylenetriamine penta acetate ($^{99m}$Tc DTPA) across the alveolar capillary barrier. Cigarette smokers have a significantly increased clearance of this solute from the lungs.4 This clearance falls toward normal within 24 hrs of stopping smoking.5,6 This rapid alteration in clearance of $^{99m}$Tc DTPA when changing smoking habits suggested that the test may be a useful guide to the pulmonary effects of changing to a lower yield cigarette.

The aim of the present study was to test the hypothesis that the abnormality in clearance of $^{99m}$Tc DTPA from the lungs of smokers would be reduced when subjects switched to cigarettes with lower yields of tobacco smoke constituents. In this context, “yields” are defined as the delivery of carbon monoxide (CO), nicotine and tar of cigarettes “smoked” by a machine set to take a 35 ml puff over 2 seconds every minute until the cigarette is smoked to within 1 cm of the filter. These are the values used to define whether a cigarette is mid-, low- or ultra-low tar and used in government publications to promote safer cigarettes. However, these “yields” may not necessarily be synonymous with the deliveries of the smoke constituents when smoked by different individuals. The investigation was carried out in two parts, because a change in the nicotine yield from a cigarette may cause the subjects to compensate by smoking more.7,8

**Material and Methods**

Both parts of this study were approved by the Northwick Park Hospital Ethical Committee. In the first part, we measured the effect on $^{99m}$Tc DTPA clearance of switching from a commercially available cigarette defined as middle tar by the Government Chemist to a commercially available low-tar cigarette. The low-tar cigarette had a reduced yield of tar, nicotine, and CO. We called this the mid-tar to low-tar study.

In the second part, we studied the effects of switching smokers between two specially manufactured cigarettes which had been formulated so that the nicotine and tar yields were similar, but in one cigarette, the CO production was reduced. This was called the mid- CO to low-CO study.

**Mid-tar to Low-tar Study**

The subjects were 20 male cigarette smokers aged 18 to 59 years (mean 30 years) with a cigarette consumption of 4-89 pack/ys (mean 25 pack/ys). All subjects normally smoked a brand of cigarette classified as middle tar by the Government Chemist. The subjects were randomly allocated to two groups. Both groups of subjects were supplied with a commonly smoked brand of middle tar (MT) cigarettes. The cigarettes were supplied at weekly intervals for the

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Table 1—Standard Machine Smoking Yields of Cigarettes Used

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<tr>
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<th>Study 1</th>
<th>Study 2</th>
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<tr>
<td></td>
<td>Mid Tar</td>
<td>Low Tar</td>
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<tr>
<td></td>
<td>(MT)</td>
<td>(LT)</td>
</tr>
<tr>
<td>Yield (mg/cigarette)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tar</td>
<td>18.0</td>
<td>9.0</td>
</tr>
<tr>
<td>Nicotine</td>
<td>1.7</td>
<td>1.0</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>18</td>
<td>10</td>
</tr>
</tbody>
</table>

Yields (ml/cigarette) were determined by the laboratory of the Government Chemist for each cigarette studied. Cigarettes were smoked under the following standard conditions: a 35 ml puff over 2 s was taken every min until the cigarette was smoked to within 1 cm of the filter.

period of the study. The subjects were asked to smoke normally and to use only the cigarettes provided. The cigarettes were packaged in identical unmarked boxes and the subjects were not informed when the change to low-tar cigarettes was made. After two weeks, one group was supplied with a commercially available brand of low tar cigarettes for the following two weeks, while the other group continued with MT cigarettes. Table 1 shows the yields of tar, nicotine and carbon monoxide for both cigarettes determined by the laboratory of the Government Chemist under the standard conditions defined in the introduction.

The half-time clearance rate of 311Tc DTPA from the lung into the blood was assessed at the end of each week for the four weeks of the study. Subjects breathed an aerosol of the tracer for three minutes while in the supine position. The tracer was generated from an Acrorn nebulizer. To ensure minimal deposition of the tracer in the airways, the output was passed through a bead separator to produce an aerosol with only 6 percent of particles >2 μm. Two scintillation detectors, one positioned over the right upper part of the chest and the other over the thigh, measured the clearance of the 311Tc DTPA from the lung to the blood and tissues. The background activity in vascular tissues within the counting field of the lung detector was subtracted as previously described. Clearance across the alveolar-capillary barrier was expressed as the time taken for the corrected activity in the lung field to fall to half its peak activity (t1/2 LB min). Each subject had a venous blood sample analyzed for carboxyhemoglobin concentration (COHb %) using an IL 282 CO-oximeter. The blood samples were taken at weeks 2 and 4 at 21:00 hrs to obtain an estimate of peak daily levels.

Mid-CO to Low-CO Study

In this study, subjects smoked the two types of specially manufactured cigarettes. Table 1 shows the yields of tar, nicotine and carbon monoxide for both types of cigarette as determined by the laboratory of the Government Chemist. Fifteen smokers, aged 23-60 years (mean 38 years) took part with a middle-tar cigarette consumption of 6-85 pack/ys (mean 25 pk/ys). The study was carried out as a double blind cross-over trial. The subjects were randomly allocated to two groups. The first group of seven subjects smoked the mid-carbon monoxide cigarette (MCO) for three weeks and were then changed to the low-carbon monoxide cigarette (LCO) for a further three weeks. The protocol for the second group of eight subjects was identical except that the order in which they smoked the cigarettes was reversed. Subjects were not informed when the changeover occurred.

Clearance of 311Tc DTPA and peak carboxyhemoglobin level were measured at the end of each week for the six-week study period. In addition, subjects were requested to collect butts of all the cigarettes smoked on the measurement day. These were counted to obtain an estimate of cigarette consumption. On the same day, subjects performed a 24-hr urine collection, an aliquot of which was analyzed for nicotine and cotinine concentration (using a modification of the method of Feyerabend and Russell) to estimate an index of total nicotine absorption.

Statistics

Mid-tar to Low-tar Study

A two-way analysis of variance was used to analyze the data for significant differences within each group. An unpaired t test was used for comparison between groups 1 and 2.

The data were analyzed for any significant correlation between t1/2LB and COHb using linear least squares regression.

Mid-CO to Low-CO Study

A two-way analysis of variance was used to compare the measured variables for the six-week study period. In addition, the mean values for weeks 2 and 3 (mid CO) were compared with the mean values for weeks 5 and 6 (low CO) using a series of t tests, as recommended for crossover trials by Hill and Armitage.

Linear least squares regression was used to identify any significant correlation between the variables measured.

For both studies a significant level of p < 0.05 was chosen.

Results

Mid-tar to Low-tar Study

There were no significant changes in 311Tc DTPA clearance (t1/2LB) in either group of subjects over the four-week period of the study (Table 2). The difference in mean values for t1/2LB between group 1 and group 2 in any of the four weeks was not statistically significant. In the group of subjects smoking middle tar cigarettes throughout the whole study period, COHb% showed no significant change between week 2 and 4. In the group who switched to low-tar cigarettes, the fall in COHb was not statistically significant (Table 2). There was a significant difference (p < 0.025) between COHb% in group 1 and 2 at week 2 but not week 4.

Table 2—T1/2LB and COHb % Mid-tar-Low-tar Study

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<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<tbody>
<tr>
<td></td>
<td>Mid Tar</td>
<td>Low Tar</td>
<td>Mid Tar</td>
<td>Low Tar</td>
</tr>
<tr>
<td></td>
<td>T1/2LB min</td>
<td>COHb %</td>
<td>T1/2LB min</td>
<td>COHb %</td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mid-mid tar</td>
<td>16.0 (7.7)</td>
<td>5.7 (1.3)</td>
<td>17.1 (5.5)</td>
<td>5.4 (1.4)</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>mid-low tar</td>
<td>21.3 (9.9)</td>
<td>8.1 (2.6)</td>
<td>20.2 (7.8)</td>
<td>7.2 (2.7)</td>
</tr>
</tbody>
</table>

Mean values (standard deviation)
Individual subject data for weeks 2 and 4 are shown in Figure 1. There was no significant correlation between COHb% and T½LB.

**Mid-CO to Low-CO Study**

The mean data for the various measures of smoke exposure (cigarette consumption, nicotine/cotinine 24-hr excretion and COHb%) together with TcDTPA clearance are shown in Table 3. There was no significant change in any of the measured variables during the six-week study period when subjects switched from the mid-CO cigarette to the low-CO cigarette or vice versa.

The data were further analyzed by comparing the mean values for weeks 2 and 3 with the mean values of weeks 5 and 6. There was no significant change in any of the variables. Individual subject data are shown in Figure 2. There was no significant correlation between the four measured variables.

The predicted reductions in CO and nicotine exposure based on the standard machine smoked yields (Table 1) were calculated:

\[
\% \text{ reduction} = 1 - \frac{\text{yield from low tar or low CO cigarette}}{\text{yield from mid tar or mid CO cigarette}} \times 100
\]

Actual reductions in CO and nicotine exposure were calculated in a similar manner from measured concentrations of blood carboxyhemoglobin and urine nicotine/cotinine excretion based on mean values for weeks 2 and 3 and weeks 5 and 6 (Table 4).

**DISCUSSION**

The aim of this study was to see if smokers who changed to cigarettes with reduced yields of tobacco smoke constituents would show any improvement in pulmonary clearance of TcDTPA. We have previously shown that the clearance of TcDTPA is abnormal in smokers and recovers towards the normal range following complete cessation of cigarette smoke exposure. Based on these data, our assumption was
that a change to a lower-yield cigarette would, in fact, produce a reduced exposure to smoke constituents and that this might be reflected in a more normal clearance rate of $^{99m}$Tc DTPA. This assumption was not confirmed in either part of this study, and the clearance half times remained within our published laboratory range for cigarette smokers: 21.3 ± 11.8 (SD) min.

The reproducibility of $^{99m}$Tc DTPA clearance measurements was determined by analyzing the difference between two measurements on the same subject made at least one week apart. In a group of 32 cigarette smokers with an average clearance of 18 min, the mean difference between duplicates was 1.0 min with a standard deviation of 4.9 min.

The most probable explanation for the lack of change in $^{99m}$Tc DTPA clearance from the lung is the failure of subjects to reduce their smoke exposure. We have previously published data demonstrating a significant hyperbolic correlation between %LB and COHb. Using this correlation, it can be calculated that the MCO group have to fall from their mean value for COHb of 6.7 percent to about 4.0 percent (a 40 percent reduction) to achieve any significant improvement in %LB. The 44 percent reductions in CO yields for cigarettes used in both studies made a change in %LB theoretically possible. However, these reductions were not achieved by subjects in each study.

A surprising finding was that in neither part of the study was there a reduction in COHb concentration when subjects smoked cigarettes with a considerably lower yield of carbon monoxide. In the first part of the study, the low tar cigarettes had a 44 percent reduction in their machine smoke yield of carbon monoxide compared to the middle tar cigarettes. If a beneficial effect of switching to lower tar cigarettes was to be achieved, we would have expected that a similar reduction in actual smoke exposure might have occurred in the LT group (Table 4). The smaller, nonsignificant fall in COHb (11 percent), suggested that smokers made some alteration in their smoking patterns to compensate for the reduced yields of tar, nicotine and carbon monoxide. A possible explanation for the compensatory increase in smoke intake in the LT group is the reduced yield of nicotine in the LT cigarette. Nicotine absorption was not measured in this first study, but other studies7,8 have shown that

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Table 4—Calculated Reductions in Carbon Monoxide and Nicotine Exposure

<table>
<thead>
<tr>
<th></th>
<th>Standard Machine Conditions (%)</th>
<th>Human Smoking Conditions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mid tar-low tar study</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>44</td>
<td>11</td>
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<tr>
<td><strong>Mid CO-low CO study</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>44</td>
<td>7</td>
</tr>
<tr>
<td>Nicotine</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>
there is a compensatory increase in nicotine absorption when subjects smoke cigarettes with a lower nicotine content. Whatever mechanism is involved to explain our data, we conclude that there was no obvious effect of switching to lower tar cigarettes on either the pulmonary clearance of $^{99m}$Tc DTPA or on smoke exposure as measured by COHb.

In an attempt to prevent possible increases in smoke intake resulting from altered nicotine yields, the second part of the study was designed so that the cigarette had similar nicotine and tar content, but differing carbon monoxide yields. In this study, the subjects showed a negligible change in nicotine/cotinine excretion when they changed from MCO to LCO cigarettes. This was predicted from the nicotine yields of the two cigarettes (Table 4) and implied that there was no compensatory increase in smoke exposure. However, the COHb concentrations only fell 7 percent instead of the expected 44 percent reduction predicted from machine-smoked values (Table 4).

The lack of change in nicotine suggested no change in smoke exposure. The failure of COHb to fall implied an increase in smoke exposure. To explain this paradox we suggest that the intake of individual components of the cigarette smoke may be regulated to achieve constant blood levels of CO and nicotine when smoking cigarettes with differing yields of CO and nicotine. Two mechanisms may be postulated. First, it has been shown that changing the air flow profiles through a cigarette can alter the ratio of nicotine to CO in the smoke$^{14}$ to produce similar nicotine yields, but doubled CO yields. Therefore, it is possible for subjects to take a puff of smoke from a cigarette so as to change the relative yields of different constituents much more than the yields estimated using standard conditions. The 50 percent difference in draw resistance between the two cigarettes (MCO 15.3 cm H$_2$O/L/min; LCO 7.6 cm H$_2$O/L/min) may have made it possible for different air flow profiles to be produced from those of the standard smoking machine.

A second explanation is that the puff of smoke taken from both the MCO and LCO cigarettes is the same as that predicted from their standard yields, but these puffs are then inhaled differently. It is known that, on average, 90 percent of the nicotine but only 60 percent of the CO is absorbed from inhaled cigarette smoke. Nicotine is absorbed from the whole of the respiratory tract, whereas CO is only absorbed from the alveoli (Creighton, DE. Paper presented at the Conference of Aerosol Physics, British American Tobacco Co Ltd, Southampton, 1973). If the depth of inhalation or the residence time of the smoke in the lungs were altered, then CO absorption would be increased to a much greater extent than nicotine absorption. This mechanism would require the presence of a “sensor” for individual smoke constituents with a feedback system to alter smoking profiles and thus to alter the absorption of individual constituents independently of the actual yield. There is no evidence available that either supports or refutes either of these suggested mechanisms.

A further possible explanation for the lack of change in $^{99m}$Tc DTPA clearance from the lung is that nicotine is inducing the abnormality. If this were the case, then as long as smokers compensate for alterations in this constituent, then no change in $^{99m}$Tc DTPA clearance would be observed despite large changes in the other constituents of the smoke. We have previously shown that oral nicotine had no effect on the rate of clearance of $^{99m}$Tc DTPA$^{16}$ although the systemic levels of nicotine achieved may not reflect what may occur if inhaled nicotine crosses the alveolar capillary membrane in greater concentration.

Our original hypothesis was that switching to lower yield cigarettes would reduce the abnormality in $^{99m}$Tc DTPA clearance observed in cigarette smokers. The lack of effect of switching cigarettes on $^{99m}$Tc DTPA clearance was due to the ability of subjects to absorb equal or larger amounts of smoke components when smoking lower yield cigarettes. Further studies to test the hypothesis that a real reduction in smoke exposure will alter $^{99m}$Tc DTPA clearance will require the development of methods to control smoke exposure. However, we conclude that the yields of cigarettes determined by the Government Chemist under standard conditions do not reliably reflect the dose of smoke inhaled by our subjects.

REFERENCES
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CHEST / 88 / 4 / OCTOBER, 1985
11 Feyerabend C, Russell MAH. Improved gas-chromatographic method and microextraction technique for the measurement of nicotine in biological fluids. J Pharm Pharmacol 1978; 31:73-6

1986 Pediatric Pulmonary Examination

The Subspecialty Committee of Pediatric Pulmonology of the American Board of Pediatrics will administer its first certifying examination on Friday, July 18, 1986.

The following criteria must be met to be eligible to sit for the examination:
1. Certification by the American Board of Pediatrics.
2. Three years of full-time subspecialty residency training in pediatric pulmonology.

OR

Five years of broadly based pediatric pulmonology. Broadly based pediatric pulmonology encompasses the majority of the clinical components which are included in the 1978 Guidelines for Pediatric Pulmonary Training (Mellins RB, Chernick V, Doershuk CF, et al: Report of the task force to establish guidelines for pediatric pulmonary training. Pediatrics 62:256-257, 1978). A minimum of 50% of all professional time must be spent in pediatric pulmonology to receive credit. All pediatric pulmonology experience must be accrued before December 31, 1990.

OR

A combination of subspecialty residency training and pediatric pulmonology experience to equal five years:
- For residencies of less than 12 months: one month of subspecialty residency training equals one month of pediatric pulmonology experience.
- For residencies of 12 to 18 months: one month of subspecialty residency training equals two months of pediatric pulmonology experience.
- For residencies of 19 to 24 months: while one month of subspecialty residency training equals two months of pediatric pulmonology experience for the first 18 months, one month of subspecialty residency training equals one month of pediatric pulmonology experience for the 19th to the 24th month.

Those entering pediatric pulmonology training in the academic year 1985-86 (on approximately July 1, 1985) must complete three years of training to qualify for admission to the examination.

3. Verification of training and/or pediatric pulmonology experience.

Each application will be considered individually and must be acceptable to the Subspecialty Committee of Pediatric Pulmonology. The Subspecialty Committee recognizes that situations may arise that are not explained by the preceding information.

Registration for this examination will extend from SEPTEMBER 1, 1985, to DECEMBER 31, 1985. Requests for applications received prior to the opening of registration will be held on file until that date at which time application materials will be sent to those who have requested them.

The application fee for the examination is $635 ($235 processing and evaluating fee + $400 examination fee). Candidates not approved to take the examination will be refunded the $400 examination fee. The processing and evaluating fee will be retained.

Please direct inquiries to the American Board of Pediatrics, 111 Silver Cedar Court, Chapel Hill, NC 27514 (919): 929-0461.