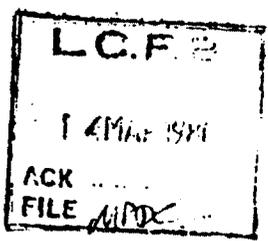


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Note for Dr. L. C. F. Blackman *LB*  
Mr. P. L. Short  
Mr. A. L. Heard  
Dr. C. I. Ayres  
Mr. P. J. Nicholl



Non-Combustible Cigarettes - "Vaping"

We have been able to learn very little further about Dr. Norman L. Jacobson, who delivered the paper on nicotine inhalation - or "vaping" - at the American College of Chest Physicians meeting at Houston last November. Jacobson comes from San Antonio, Texas, but little else seems to be known about him.

However, we were lent a cassette recording of his talk (which has been duplicated and is available, if needed, although the sound quality is poor). A transcript of the talk is appended for your information.

D. G. FELTON

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13th March, 1980

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Presentation by Dr. Norman L. Jacobson of San Antonio to a meeting of the American College of Chest Physicians at Houston on 4-8th November, 1979.

Non-combustible Cigarette:  
Alternative Method of Nicotine Delivery

Good Morning, Chairman, Colleagues.

Now I am about to propose a cigarette for an alternative method of nicotine delivery. If nicotine is truly addicting and if tar, carbon monoxide and other by-products of smoking are injurious to health, then obviously, it would be beneficial to develop a cigarette which supplies nicotine, but eliminates the other toxic ingredients. Numerous efforts to deliver nicotine only through other vehicles including nicotine tablets, injections, aerosols and gum have been partially successful, but have been found impractical or unsatisfying.

This presentation describes a practical and apparently satisfying method of administering nicotine by nicotine vapour inhalation via a non-combustible cigarette, hereafter referred to as an NCC. To our knowledge, a method of inhaling pure nicotine vapour has not been reported previously. To simplify description, we will hereafter refer to nicotine vapour inhalation through an NCC as vaping and people who inhale nicotine vapour as vapers.

The NCC closely approximates the size and appearance of a standard cigarette. It allows a slightly impeded flow of inhaled air and is designed to deliver approximately 50 µg of nicotine per 300 cc of inhalation. This is approximately half of the quantity of nicotine delivered from each cigarette puff. The difference between cigarette smoking and inhaling nicotine vapour through an NCC requires description. Cigarette smoking consists of a bolus of smoke, approximately 30-50 cc in size, drawn into the mouth and held and subsequently inhaled and dispersed throughout the lungs. Vaping represents the immediate inhalation of 3-400 cc of nicotine laced air directly into the lungs.

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In this study, six subjects were tested over nine consecutive days. Cigarettes only were smoked ad libitum on days 1 thro 9 and NCC's only were inhaled ad libitum on days 4 thro 9. Blood carboxyhaemoglobin levels were determined daily to verify that subjects were either smoking standard cigarettes or not smoking cigarettes. 24 hour urines for cotinine were collected daily and measured by gas chromatography. Cotinine is the main metabolite of nicotine and is used as an estimate for total nicotine consumption. Serum nicotine estimations were performed using a regular immunoassay method on the second and third day of cigarette smoking and on the last two days of NCC inhalation. The test results reliability were checked in the usual fashion using split samples and controls containing known quantities of nicotine and cotinine. Carboxyhaemoglobin levels during cigarette smoking varied between 3.3% and 8.6%, with an average of 5%. These levels are consistent with carbon monoxide measurements in other smoking studies.

Following conversion, NCC's on day 4 of the experiment, the daily average level promptly dropped 0.8%, a level consistent with non smokers. 24 hour urine cotinine excretion varied between 1.9 and 5.8 mgs during cigarette smoking, which are levels similar to those recorded in other smoking studies. Between 0.4 and 8.6 mgs of cotinine were excreted by using NCC's. The highest urine cotinine levels on cigarettes and NCC's were in the most experienced vaper. Four subjects, 2 naive vapers and 2 experienced vapers, excreted less cotinine with NCC's than with cigarettes. These four subjects gradually reduced their urine cotinine excretion after changing from standard cigarettes to NCC's, until reaching their rather fixed daily excretion rate. This raises the possibility that less nicotine is required from a pure vapour source to provide equivalent satisfaction in some people. One experienced vaper excreted similar quantities of nicotine with NCC's and cigarettes and another excreted more nicotine - excuse me - cotinine with NCC's. The two high cotinine excretors demonstrated widely variable daily cotinine excretions. A learning factor may exist, as a subsequent study on one of the naive vapers yielded substantially higher cotinine and nicotine levels. Serum nicotine levels were measured before, 2 minutes after and 5 minutes after smoking a 1.2 mg nicotine Lark filter cigarette for a 10 minute period

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Serum nicotine levels 2 minutes after smoking rose to an average of 40.5 ng per ml on the second day and 48 ng per ml on the third day. This corresponds to values obtained by other workers. Changing from the puffing technique for cigarette smoking to nicotine vapour inhalation was easily accomplished by all subjects. No serum nicotine measurements were made on days 4 through 7 in order to permit practice vaping. Serum for nicotine was collected on the 8th and 9th day at 2 hour intervals between 9 a.m. and 7 p.m. The 11 a.m., 3 p.m. and 7 p.m. specimens were secured randomly and the 9 a.m., 1 p.m. and 5 p.m. specimens were secured 2 minutes after inhaling nicotine through the NCC every 30 seconds for 10 minutes. The figure shows a rather haphazard array of nicotine levels. Each subject demonstrated a wide variation of results on both days. There was also a wide range of average nicotine levels among the subjects. Plateau effect was not demonstrated. The peaking and trough patterns did not consistently correspond to the alternating programmed nicotine inhalation and random sampling. There was no definite relationship between the levels of serum nicotine reached while smoking cigarettes and those while vaping. For example, the subject represented by the open square averaged 35 ng per ml at 2 minutes after smoking a cigarette and averaged 50 ng per ml while vaping. On the other hand, the subject represented by the solid triangle averaged 59 ng per ml at 2 minutes after smoking and only 23 ng per ml while vaping.

No side effects occurred with normal NCC usage. In an acute study, one experienced vaper's efforts to reach toxic levels of nicotine with rapid inhalation of nicotine vapour, produced hiccups at a comparatively low serum nicotine level of 25 ng per ml. No hiccups occurred, though faintness did, with rapid forced cigarette smoking, which produced a very high serum nicotine level of 149 ng per ml. Similar blood pressure elevations and increased pulse rates were demonstrated with forced vaping and smoking. It is noteworthy that nicotine gum chewing also produces numerous side effects including hiccups at levels lower than or equivalent to cigarette smoking.

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These findings imply that smoking reduces the appearance of nicotine side effects through an undefined mechanism. Perhaps carbon monoxide or other products of pyrolysis suppress central nervous system nicotine receptors or otherwise alter the autonomic nervous system. If so, smoking may suffer the additional stigma of reducing the body's response to nicotine and consequently increasing the nicotine requirement to produce desired physiologic responses.

Nicotine inhalation seems satisfying and the four experienced vapers are far more heavy cigarette smokers and presently are inveterate vapers or can easily transfer between NCC's and cigarettes. The two subjects who were first exposed to NCC's during this study, minimised or eliminated their cigarette consumption while on study and continued vaping until their supply of NCC's was halted.

We have demonstrated that nicotine vapour can be inhaled and that meaningful levels of serum nicotine and urine cotinine are achieved by inhalation. Nicotine vapour inhalation varies from person to person as does nicotine consumption vary among cigarette smokers. It is likely that experienced vapers will titrate their inhalation to maintain a certain nicotine level in the same fashion as cigarette smokers. The vapers have the advantage of vaping while working, attending class and flying, since there are no noxious fumes and odours to offend non smokers. If NCC's are widely accepted, it will substantiate the growing conviction that nicotine alone is the habituating ingredient in cigarette smoking. Subsequently, it will be necessary to determine if inhaling NCC causes a reduction of diseases attributed to cigarette smoking. Since it is likely that nicotine alone produces long term harmful effects, the NCC does not represent a safe cigarette, but it may be a worthy alternative to the standard tobacco cigarette. Thank you.

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Questions and Answers

Hassan (?) from Philadelphia

Q. What do you ..... in this study, you just had the subjects with cigarette smoking and vapour smoking?

A. That is correct.

Q. Norman. There has been a lot of trial nicotine gum as a technique to help people stop smoking. Can you vary the amount of nicotine or gradually taper off the nicotine content of NCC's? Would it be a viable tool perhaps for smokers cessation?

A. Yes. That is in our expense(?) department.

They are not expensive, you know, as an experimental tool, at this point, so really it is hard to define the cost, but, Yes, the dosage can be varied and of course, nicotine chewing gum has had a few problems:

1. It is not socially ideal. It is hard to feature lawyers and bankers at meetings chewing gum and also you know the problem of getting a bolus or an adequate dose of nicotine by chewing gum. It is not as effective as inhalation, which is a more rapid and effective way of administering nicotine and furthermore, nicotine chewing gum tends to have side effects, as Russell has shown.

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