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Variations in Carboxyhaemoglobin Levels in Smokers

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Summary

Three experiments on smokers have been performed to determine variations in blood levels of carboxyhaemoglobin (COHb) throughout the day and night and whether a random measurement of COHb gives a true estimation of a smoker's mean COHb level. In the individual smoker the COHb level does not increase gradually during the day but is kept within relatively narrow limits. Moderately heavy smokers rise in the morning with a substantially raised COHb level because the half life of COHb is significantly longer during sleep than during the day. Women excrete their carbon monoxide faster than men. A random COHb estimation gives a good indication of the mean COHb level of an individual.

Introduction

The inhalation of tobacco smoke containing up to 5% carbon monoxide can substantially raise the level of carboxyhaemoglobin (COHb) in the blood (Goldsmith and Landaw, 1968; Cole *et al.*, 1972). Levels of up to 16% have been recorded in cigarette smokers (Lawther and Commings, 1970), and the COHb level of inhaling smokers is significantly higher than that of non-smokers (Castleden and Cole, 1974). The COHb level can thus identify those people at risk from any of the diseases associated with the inhalation of tobacco smoke even if carbon monoxide is not directly implicated in the pathogenesis of those diseases. For such identification, however, a doctor must know what relationship the random COHb estimation in patients at risk bears to the average COHb level throughout the day, to the time interval from the last cigarette, and to the activity of the patient.

Astrup (1972) has shown that a much greater degree of atherosclerosis can be induced in the aortas of cholesterol-fed rabbits when exposed to continuous carbon monoxide and air rather than to air alone. As man eats a substantial amount of cholesterol he may be subjecting himself to similar pathogenic stimuli as the rabbits if he maintains a constant level of COHb.

We therefore investigated the variation in the COHb of a moderately heavy smoker throughout 24 hours, the relationship between the rate of elimination of COHb and level of activity, and whether a random COHb estimation in a smoker gives a true estimation of his mean COHb level.

Methods

Four smokers, two men and two women, were studied for 12 hours on one day. Their COHb was estimated immediately before and after each cigarette, but they smoked entirely as they wished. They did not smoke from the time they went to bed until an indwelling venous cannula was inserted the next morning on arrival in the laboratory.

A further six volunteers had several blood samples taken on one day. They were allowed to smoke as they wished, and they carried on their normal daily activities. Each subject chose when he provided the blood sample so long as it was not within one hour of the previous sample or within half an hour of having smoked a cigarette.

Finally, nine subjects, four men and five women, were asked to smoke their usual number of cigarettes between waking and 11.00 hours. They then had no further cigarettes for four hours and, after 30 minutes, blood samples were taken every half an hour. Light activity involving moving around a room was allowed in this period. After four hours they were allowed to smoke as they wished. Each subject was provided with a means of collecting a further sample of blood immediately before sleep and immediately on waking the next morning.

All volunteers regularly smoked more than 10 cigarettes a day. All COHb values were estimated from venous blood samples as previously described (Castleden and Cole, 1973).

Results

The mean initial COHb level in the morning of the four subjects in the first experiment was 3.2%. Though the COHb invariably rose with every cigarette smoked (mean rise 1.3%) and always

FIG. 1—Effect of cigarette smoking on carboxyhaemoglobin (COHb) level in four subjects. Levels were estimated immediately before and after each cigarette.

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Half Life of Carboxyhaemoglobin in Hours in Four Men and Five Women in Day Time and at Night

	Men					Women					
Subject No.:	11	12	13	14	Mean	15	16	17	18	19	Mean
Day	4.00	3.25	5.75	2.75	3.94	2.25	2.25	2.25	2.75	2.25	2.35
Night	11.75	6.75	10.00	7.25	8.94	5.25	5.00	6.50	3.50	6.50	5.35

fell between cigarettes it remained within 1% COHb of the mean daily level for that subject (fig. 1). This did not include the period when the subject was actually smoking or within half an hour of finishing a cigarette nor the early part of the day. Most cigarettes (83%) were lit when the COHb had fallen below the subject's mean COHb level. Nevertheless, in this small group there was no significant difference in the increase of COHb, between times when the cigarette was lit above (average 1.1%) and times it was lit below (average 1.4%) his mean.

The results of the second experiment showed that (a) each subject kept his COHb within narrow limits in a similar manner to the first group; (b) a random COHb level at any time during the day—except at the times specified above—gave a good indication of the mean COHb level maintained by that subject; and (c) the COHb level did not rise progressively throughout the day even if the subject smoked more than 30 cigarettes (subject 5; fig. 2).

FIG. 2—Random carboxyhaemoglobin (COHb) levels in six subjects. Samples were collected at times determined by subjects but not within half an hour of lighting cigarette.

FIG. 3—Different rates of fall of carboxyhaemoglobin (COHb) during two periods when subject 11 was not smoking.

In every subject in the third experiment the half life of COHb during sleep (mean 6.9 hours) was substantially longer than that during the day (3.1 hours) (see table). This difference was highly

significant ($P < 0.001$). The different rates of fall of COHb during the two periods in which one subject (11) was not smoking are shown in fig. 3. We assumed that the fall during the night was exponential, as it was during the day. The pattern shown in fig. 3 was typical for all the subjects in the experiment. Both at night and during the day women excreted their carbon monoxide at a significantly faster rate than men ($P < 0.025$).

Discussion

Our results suggest that in the individual smoker the COHb level is fairly constant throughout 24 hours and does not normally rise to a maximum at the end of the day. On theoretical grounds it might be argued that such results are not altogether unexpected. It is known that the rate of elimination of COHb is proportional to the activity of the subject: the greater the activity, the faster the elimination (Forbes *et al.*, 1954; Coburn *et al.*, 1965; Shields, 1971). It can be inferred, therefore, that the rate of elimination in any one subject is substantially slower during sleep than during the day. Thus, a heavy smoker may well rise in the morning with a COHb level already higher than would be found in a non-smoker. Furthermore, as nicotine is mainly absorbed from cigarette smoke by the lower respiratory mucosa a cigarette smoker must inhale to obtain a satisfactory blood level of nicotine (Armitage and Turner, 1970). The amount he inhales is reflected directly by his COHb level. If, therefore, he needs a constant level of nicotine in his blood it would be surprising to find that the COHb level rose progressively during the day, as some authors have suggested (Russell *et al.*, 1973).

In four subjects we measured the COHb before and after each cigarette over a period of 12 hours. It can be seen from fig. 1 that the COHb fluctuates about a mean for each subject, the actual level being set by his cigarette consumption. An exception to this is found only during the first part of the day, while the subject is smoking, or within half an hour of finishing a cigarette. This is because it takes about half an hour for the carbon monoxide to be equally distributed throughout the extravascular compartments of the body (Coburn, 1970). This has been ignored by some investigators and may explain the discrepancy between their results and ours (Cohen *et al.*, 1971; Russell *et al.*, 1973). Our results agree with those of McIlvaine *et al.* (1969), who measured the COHb at specific times and not immediately after smoking a cigarette.

Further evidence that each smoker maintains his COHb at a constant level came from our study of six working volunteers. Random samples of their blood taken during their working day showed no progressive increase in COHb during the day and a small and characteristic range of results for each individual (fig. 2).

These results confirm that a smoker attempts to maintain a constant blood level of some substance found in cigarette smoke. On present evidence this is most likely to be nicotine (Russell, 1974).

Having established that the COHb level remains fairly constant in a heavy smoker during the day we have further shown that the level is substantially raised for much of the night. Nine subjects retired to bed with a mean COHb level of 8.0%. They woke after an average of seven and three-quarter hours of sleep with a mean COHb level of 3.7%, which was significantly higher than we found in non-smokers working in the City of London (Castleden and Cole, 1974). As the rate of elimination of carbon monoxide is proportional to alveolar ventilation these results

were not entirely unexpected (Forbes *et al.*, 1945; Coburn *et al.*, 1965; Shields, 1971). The fact that women eliminate their carbon monoxide faster than men, both at night and during the day, however, was surprising though agreeing with the results of Godin and Shephard (1972). A possible explanation for these results may be that men have more binding sites for carbon monoxide—that is, they have a larger myoglobin and haemoglobin mass. It follows, therefore, that a man will have a larger absolute amount of carbon monoxide than a woman for the same COHb level expressed as a percentage of the total haemoglobin.

Hence, a random COHb estimation shows the approximate mean COHb level which the subject maintains throughout 24 hours, and heavy smokers are continuously at risk from any adverse effects of carbon monoxide. They are therefore subjecting themselves to similar atherogenic stimuli as Astrup's experimental animals.

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Studies on Whole-body Potassium in Non-ketoacidotic Diabetics Before and After Treatment

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Summary

Serial measurements of whole-body potassium were carried out in 28 diabetic patients, in 23 of whom diabetes had only recently been diagnosed. Eleven patients were treated with insulin, 12 with oral hypoglycaemic agents, and the rest were already on oral hypoglycaemic agents and had developed poor diabetic control; four of these required insulin. Whole-body potassium was measured before treatment was begun (or altered) and again one and six weeks later. Whole-body potassium (ratio of observed to expected) was initially reduced in most of the patients requiring insulin. After control of diabetes whole-body potassium increased significantly in the three groups. The increase in whole-body potassium in the individual patients varied over a wide range, and in patients who were treated with insulin it was often of a similar magnitude to that observed in patients in diabetic ketoacidosis.

Introduction

Metabolic balance studies have shown that patients in diabetic ketoacidosis may be severely depleted of potassium (Danowski *et al.*, 1949; Nabarro *et al.*, 1952). Less is known, however, about the potassium status of patients who have uncontrolled

diabetes but are not ketoacidotic. Some information has been obtained through the studies of exchangeable potassium (Aikawa *et al.*, 1953; Telfer, 1966), a technique which has limitations not only because it is time consuming but also because it involves exposure of the subject to radiation.

Determination of the naturally occurring radioactive isotope of potassium-40 with the whole-body counter has certain advantages over both balance studies and exchangeable potassium techniques. It can be done quickly on an outpatient basis, thus making serial studies relatively easy, and because naturally occurring ^{40}K is measured radiation exposure is avoided. We have carried out serial measurements of whole-body potassium in non-ketoacidotic patients using the whole-body counter. The patients were newly diagnosed, untreated diabetics as well as established diabetics with poor control. The objectives of the study were to determine the potassium status of diabetic patients with uncontrolled diabetes, and to determine the effect of improvement of diabetic control on whole-body potassium.

Patients

Twenty-eight patients were investigated. Of these 23 were newly-diagnosed diabetics who had been referred to the diabetic clinic, diabetes being confirmed by a random blood sugar of over 200 mg/100 ml in association with symptoms of diabetes. Five patients who had established diabetes treated with oral hypoglycaemic agents were also investigated. In these cases symptoms of poor diabetic control had developed and heavy glycosuria had been present persistently for a month or more. No patient was clinically ketoacidotic and none had ketonuria. Each of the 28 patients had a whole-body potassium measurement before treatment was begun (or altered in the case of the patients already on treatment). The 23 new diabetics were then put on an appropriate carbohydrate-restricted diet and, using ordinary clinical criteria, 11 of them were treated with insulin and the remainder with oral hypoglycaemic agents (eight with sulphonylureas and four with biguanides). Of the five established diabetics who had uncontrolled diabetes four were put on insulin and one who was on sulphonylureas was given biguanides in addition. All patients had further whole-body potassium measurements one and six weeks later.

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