A Comparison between Carboxyhemoglobin and Serum Thiocyanate Determinations as Indicators of Cigarette Smoking

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Abstract: Cigarette smoking histories were compared to carboxyhemoglobin and serum thiocyanate concentrations obtained from 426 smokers and 191 non-smokers. The mean levels of both carboxyhemoglobin and serum thiocyanate were significantly higher among cigarette smokers and correlated with the number of cigarettes smoked per day. The specificity of both procedures was 81 per cent, and serum thiocyanate had a higher sensitivity (93 per cent vs. 83 per cent), making it potentially more suitable for use as an index of cigarette smoking. (*Am J Public Health* 70:284–286, 1980.)

Introduction

Assessment of the effectiveness of smoking cessation programs has generally relied upon data reported by the participants and are thereby subject to considerable bias.[1–4] Smokers in such programs who have failed to stop smoking or reduce their cigarette consumption may under-report the number of cigarettes they smoke per day to avoid the risk of disappointing an intervention staff and the embarrassment of failure. Independent measures of cigarette smoking are therefore necessary to objectively evaluate the results of anti-smoking activities.

Previous studies have shown that carboxyhemoglobin[1–5] and serum thiocyanate levels[6–10] are higher in cigarette smokers and that these determinations may be helpful in distinguishing smokers from non-smokers. We recently had the opportunity to compare these two methods with responses to an inquiry about cigarette smoking obtained during the screening phase of the Multiple Risk Factor Intervention Trial (MRFIT).[11]

Methods

As part of the screening procedure for the MRFIT in St. Louis, Missouri, male volunteers between the ages of 35–57 years were asked to complete a short form which included the following question: "On the average how many cigarettes do you smoke a day?" Men who were at above average risk for coronary heart disease[12] were invited to attend a second screening visit. Because the men were instructed to fast for at least 12 hours, this visit was usually scheduled for the morning. In the course of the examination, blood specimens were obtained for measurement of carboxyhemoglobin and serum thiocyanate levels. Smoking prior to this examination was not prohibited although smoking was not permitted within the clinical center. The time interval since the last cigarette was not determined. Serum thiocyanate determinations were performed at the MRFIT central laboratory facility using an automated colorimetric assay.[9] Carboxyhemoglobin levels were measured locally using an Instrument Laboratories 182-CO-Oximeter.[13] Men who were not excluded at the second screen examination were asked to return for a third visit. No advice or recommendations relating to risk factors were given to these men at these visits. The data presented below are the results of the carboxyhemoglobin and serum thiocyanate levels determined at the second screening visit compared to the smoking histories obtained at the first visit. Change in the smoking habit between these visits was small and is not considered in the data analysis.

Results

The frequency distributions of the carboxyhemoglobin and serum thiocyanate levels for the 191 non-smokers and 426 cigarette smokers based on their responses to the smoking question are shown in Figures 1 and 2 respectively. The mean carboxyhemoglobin level for non-smokers was 1.1 ± 1.4% (S.D.) and for smokers, 4.5 ± 2.5 per cent. For non-smokers, the mean serum thiocyanate level was 73.5 ± 48.3 μm/l; for smokers the mean concentration was 180.2 ± 55/7 μm/l. The differences between the mean levels for smokers and non-smokers of both carboxyhemoglobin and serum thiocyanate are highly significant ($p < .001$).

The level of carboxyhemoglobin which best discriminates between smokers and non-smokers is 2 per cent and this cut-point yields a copositivity (sensitivity) and conegativity (specificity) of 83 per cent and 81 per cent respectively. For serum thiocyanate, the best discriminating level is 100 μm/l, and this provides a copositivity of 93 per cent and conegativity of 81 per cent.

The relationship between carboxyhemoglobin and serum thiocyanate concentrations and the average number

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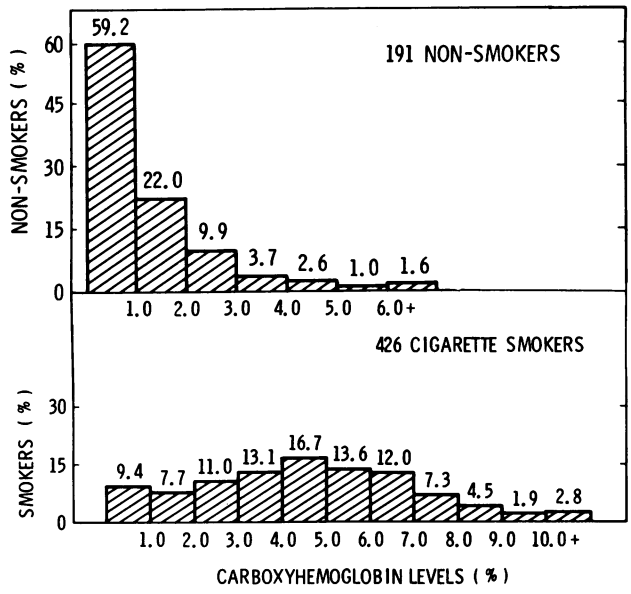

FIGURE 1—Frequency Distribution of Carboxyhemoglobin Levels

of cigarettes smoked per day is shown in Figure 3. There is a progressive rise in the levels of both carboxyhemoglobin and serum thiocyanate with increasing cigarette consumption. Among smokers, the correlation coefficient for the number of cigarettes smoked per day vs carboxyhemoglobin is 0.29, and for thiocyanate, r = 0.25. The correlation coefficient for carboxyhemoglobin vs serum thiocyanate is 0.37. All of these correlation coefficients are statistically significant ($p < .01$).

Discussion

Our data are consistent with previous studies which have shown both carboxyhemoglobin and serum thiocyanate

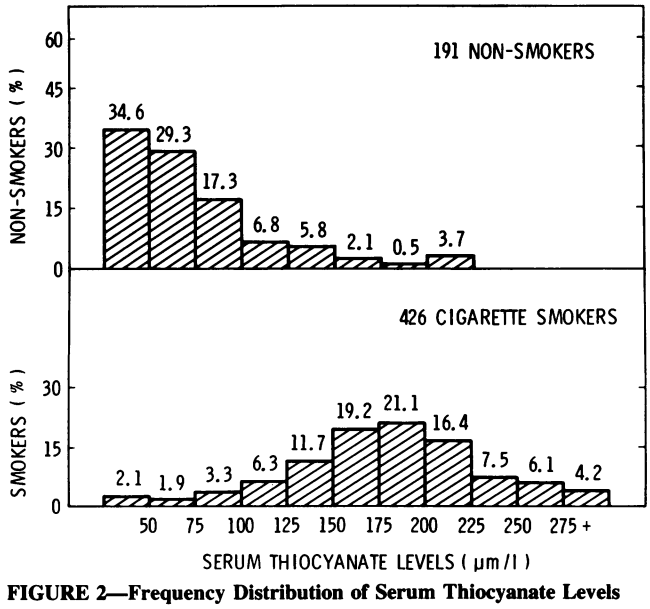

FIGURE 2—Frequency Distribution of Serum Thiocyanate Levels

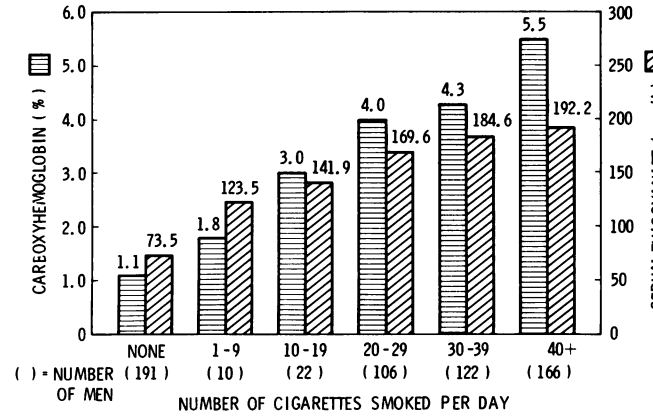

FIGURE 3—Relationship between Mean Carboxyhemoglobin, Serum Thiocyanate and the Number of Cigarettes Smoked per Day

levels to be significantly higher among cigarette smokers and non-smokers.[1-10] In direct comparison of these two measures we find no difference in specificity and a higher sensitivity for the thiocyanate determination which is probably due to its much longer half-life—14 days vs 4 hours for carbon monoxide.[14, 15] A serum thiocyanate determination would therefore be more likely to identify a smoker who has not smoked for 8–12 hours as would be the case for smokers scheduled for morning health examinations who elect not to smoke prior to the visit.

The only previously reported direct comparison of CO exposure and thiocyanate was by Vogt et al,[10] who measured expired air CO rather than carboxyhemoglobin but these two measures are highly correlated with one another.[15] The values of the present study are very close to those cited in the Vogt study but differ sightly in that the correlations between reported levels of smoking among the 94 cigarette users in that study were higher for both expired air CO levels (r = .48) and serum thiocyanate (r = .48). In addition, although the sensitivities and specificities were not reported in the earlier study, calculations from their Table 3 yield a slightly higher sensitivity for expired air CO (88 per cent) than for serum thiocyanate (81 per cent) and also a higher specificity (93 per cent vs 83 per cent). Our study included pipe and cigar smokers and categorized them by their cigarette smoking habit, while the Vogt study excluded pipe and cigar smokers. This difference in methodology probably contributes in part to the differences in the findings of the two studies. In addition, variation in exposure to environmental sources of both carbon monoxide and thiocyanate may account for differences in the specificities of these measurements. Atmospheric pollution, principally from motor exhaust fumes, is the major source of environmental carbon monoxide and can cause elevation of the carboxyhemoglobin levels.[5] Thiocyanate is mainly derived from plants[16, 17] and vegetarians have higher serum thiocyanate levels than non-vegetarians among smokers and non-smokers.[8] Differences in exposure to these environmental sources of both CO and thiocyanate between population groups can thus effect the validity of these measures as an index of cigarette smoking.

These data confirm and extend the findings of earlier

studies and suggest that both carboxyhemoglobin and serum thiocyanate measurements may be useful in distinguishing cigarette smokers from non-smokers. However, the measurement of the thiocyanate concentration in the serum appears to be the preferable method because of its longer half-life which provides the basis for a more sensitive index, the relative ease of handling serum and the availability of a simple, automated method of analysis.

REFERENCES

1. Delarue NC: A study in smoking withdrawal. Can J Pub Health 64:S5-S19, 1973.
2. Ohlin P, Lundh B, Westling H: Carbon monoxide blood levels and reported cessation of smoking. Psychopharmacology 49:263-265, 1976.
3. Isacsson SO, Janzon L: Results of a quit-smoking research project in a randomly selected population. Scand J Soc Med 4:25-29, 1976.
4. Sillet RW, Wilson WB, Malcolm RE, et al: Deception among smokers. Brit Med J 2:1185-1186, 1978.
5. Stewart RD, Baretta ED, Platte LR, et al: Carboxyhemoglobin levels in American blood donors. JAMA 229:1187-1195, 1974.
6. Wilson J, Matthews DM: Metabolic interrelationships between cyanide, thiocyanate and vitamin B_{12} in smokers and non-smokers. Clin Sci 31:1-7, 1966.
7. Densen PM, Davidow B, Bass HE, et al: A chemical test for smoking exposure. Arch Environ Health 14:865-874, 1967.
8. Dastur DK, Quadros EV, Wadia NH, et al: Effect of vegetarianism and smoking on vitamin B_{12}, thiocyanate, and folate levels in the blood of normal subjects. Brit Med J 3:260-263, 1972.
9. Butts WC, Kuehneman M, Widdowson GM: Automated method for determining serum thiocyanate, to distinguish smokers from non-smokers. Clin Chem 20:1344-1348, 1974.
10. Vogt TM, Selvin S, Widdowson GM, et al: Expired air carbon monoxide and serum thiocyanate as objective measures of cigarette exposure. Am J Public Health 67:545-549, 1977.
11. The Multiple Risk Factor Intervention Trial (MRFIT): The Multiple Risk Factor Intervention Trial Group. JAMA 235:825-827, 1976.
12. Statistical design considerations in the NHLI Multiple Risk Factor Intervention Trial (MRFIT). The Multiple Risk Factor Intervention Trial Group. J Chron Dis 30:261-275, 1977.
13. Maas AH, Hamelink ML, DeLeeuw RJ: An evaluation of the spectrophotometric determination of HbO_2, HbCO and Hb in blood with the Co-Oximeter IL 182. Clinica Chimica Acta 29:303-309, 1970.
14. Pettigrew AR, Fell GS: Simplified colorimetric determination of thiocyanate in biological fluids and its application to investigation of the toxic amblyopias. Clinical Chemistry 18:996-1000, 1972.
15. Landaw SA: The effects of cigarette smoking on total body burden and excretion rates of carbon monoxide. J Occup Med 15:231-235, 1973.
16. Langer P, Greer MA: Antithyroid Substances and Naturally Occurring Goitrogens. New York: S. Karger, 1977.
17. Pechacek TF, Luepher RV, Jacobs DS, et al: Effect of diet and smoking on serum and saliva thiocyanates. Presented at AHA Conference on cardiovascular epidemiology, New Orleans, 1979.

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Workshop on Heart Attack Prevention: Practical Guides to Risk Factor Reduction

The Laboratory of Physiological Hygiene of the University of Minnesota and the Minnesota Affiliate of the American Heart Association will present a workshop on "Heart Attack Prevention" June 2-4, 1980, at Spring Hill Center in Minneapolis. Medical Practitioners and allied health professionals who participate in these programs are expected to:

1. Acquire skills needed to help patients reduce risk factors for cardiovascular disease.
2. Through demonstration and guided practice, incorporate practical methods for modifying eating patterns, blood lipid and blood pressure levels, smoking habits, body weight, and physical activity levels in patient care.

These workshops will be of particular interest to physicians and supporting health professionals to include nurses, physicians' assistants, dietitians and nutritionists. A limited number of "Team" registrations are available. For more information, please contact: Lori Wheatcroft, Office of Continuing Medical Education, University of Minnesota Medical School, Box 293 Mayo Memorial Building, 420 Delaware Street, SE, Minneapolis, MN 55455.

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