Effect of Smoking on the Fasting Blood Sugar and Pressor Amines

By Kai Rehder, M.D., and Grace M. Roth, Ph.D.

When 24 normal subjects under basal conditions smoked two thirds of 2 cigarettes, there was no appreciable rise in the levels of the fasting blood sugar and the epinephrine-like substances of the systemic venous blood. However, the smoking of two thirds of 2 cigarettes significantly raised the blood pressure and pulse rate, and decreased the skin temperature of fingers and toes.

EVIDENCE has been presented by various investigators that smoking of cigarettes causes transient hyperglycemia in human beings. Haggard and Greenberg, Caponnette, Töppner, Burstein and Goldenberg, and Lundberg and Thyselius-Lundberg found in nondiabetic habitual smokers an increase in the level of the fasting blood sugar after smoking and a similar effect was produced by intramuscular injection of nicotine in some animals studied but not in all. The parenteral injection of various amounts of nicotine into animals caused a mild to moderate transient hyperglycemia according to Nicolaysen, Leloir, Wilson and DeEds, Mosinger and associates, Kobayashi, and Hazard and Vaille.

On the other hand, there is also evidence that a change in the concentration of blood sugar does not take place after smoking. Dill, Edwards, and Forbes reported that 90 per cent of their 60 subjects did not have a significant increase in the level of the fasting blood sugar after smoking. Furthermore, Cristol could demonstrate no change in the level of the fasting blood sugar in 175 medical students after each had smoked three fourths of 2 cigarettes. Ssalischtscheff was the only investigator who observed hypoglycemia during smoking by 5 nonsmokers and 6 smokers, but all his subjects showed signs of nicotine intoxication when the determinations of the blood sugar were done.

The question arose as to whether the blood sugar in normal persons who smoked habitually could be significantly elevated by smoking. Because this elevation has been suggested by Kobayashi, Leloir, and Haggard and Greenberg to result from the discharge from the adrenal gland of epinephrine or noradrenaline on smoking, the present investigation was begun.

METHODS

Blood sugar, pressor amines in the plasma, skin temperatures of the fingers and toes, blood pressures and pulse rates were determined before and after smoking on 24 male subjects (all physicians) whose ages ranged from 26 to 35 years.

Preliminary Studies. The subjects fasted for 15 hours before the tests, and during the tests they wore lightweight shorts and T shirts and were in a supine position on a comfortable bed in a constant temperature room at 25.5 C. with a relative humidity of 40 per cent. All unnecessary noises and other stimuli likely to cause vasoconstriction were excluded during the test.

The skin temperatures of the planter surfaces of the first and third toes of both feet and the volar sides of the distal phalanges of the first and third fingers of both hands were measured by means of copper constantin thermocouples designed by Sheard at 10-minute intervals for an hour. During this time the basal metabolic rate was determined, and the blood pressures and pulse rates were measured at 10-minute intervals.

When the skin temperature, blood pressure, and pulse rate were fairly well stabilized, a siliconized needle was inserted into an antecubital vein, and without the use of a tourniquet 3 samples of blood of 1 ml. each were collected at intervals of 1 minute. An additional sample of 15 ml. of blood was withdrawn for the determination of the pressor amines.

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Blood Sugar and Epinephrine-like Substances. The determinations of fasting blood sugar were carried out in duplicate by the Somogyi-Nelson method. This method was used because it measures only glucose in contrast to the Folin-Wu and Hagedorn-Jensen methods, which measure all reducing substances in the blood. The blood for determination of sugar was rendered incoagulable by adding 2 drops of heparin to each 1 ml. and by keeping it in a refrigerator during the test. The pressor amines in plasma were estimated as total epinephrine-like substances by the method of Weil-Malherbe and Bone.

Smoking. The subjects then smoked in succession two thirds of each of 2 filtered cigarettes. All but one inhaled the smoke with the depth and frequency to which they were accustomed. The blood pressure, pulse rate, and skin temperature were determined simultaneously at intervals of 1 minute during the smoking, which lasted 6 to 17 minutes, and for 13 to 24 minutes after smoking had ceased. At intervals of 3, 5, 10 and 15 minutes after smoking was begun, 1 ml. of blood was drawn for determinations of blood sugar and 15 ml. of blood was obtained between the third and fifth minutes for determination of the pressor amines. A final sample for determination of pressor amines was taken 15 minutes after smoking had ceased.

Cold Pressor Test. A cold pressor test was performed on each individual after the study was finished.

Control Group. Another 3 subjects were tested under essentially the same circumstances without smoking. They served as a control group.

Results

Blood Sugar. A total of 382 determinations of fasting blood sugar were performed on 24 healthy male individuals, 146 prior to smoking, 158 during smoking, and 78 after smoking. An additional 40 determinations were carried out on 3 subjects who did not smoke and served as a control group. No change in the mean level of the fasting blood sugar was observed before, during and after smoking (table 1). The mean values for blood sugar before smoking ranged from 69.0 ± 1.0 to 67.0 ± 1.0 mg. per 100 ml., and during and after smoking from 68.0 ± 1.0 to 69.0 ± 1.0 mg. per 100 ml. The maximal observed increase of the blood sugar during smoking was 9 mg. per 100 ml. and the maximal decrease was 10 mg.

<table>
<thead>
<tr>
<th>Time (min.)</th>
<th>Blood sugar (mg. per 100 ml.) Mean ± S.D.</th>
<th>Epinephrine-like substances (μg. per 100 ml.) Mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before smoking</td>
<td>24.0 ± 0.2 1</td>
<td>24.0 ± 0.2 1</td>
</tr>
<tr>
<td>During smoking</td>
<td>68.0 ± 1.0 9.0</td>
<td>68.0 ± 1.0 9.0</td>
</tr>
<tr>
<td>After smoking</td>
<td>69.0 ± 1.0 8.0</td>
<td>69.0 ± 1.0 8.0</td>
</tr>
</tbody>
</table>

*The number following the ± is the standard error of the mean.
†S.D., standard deviation.

In one study the second cigarette was not offered until the skin temperature had almost reached its normal value. This corresponded to an interval of 30 minutes between the 2 cigarettes. Again, we were unable to find any significant hyperglycemia. In 2 further studies, determinations of blood sugar were carried out 46 minutes after the patient finished smoking. Again no definite increase of the level of the blood glucose could be detected. The mean level for blood sugar of the control group who did not smoke ranged from 71.0 ± 2.0 to 74.0 ± 2.0 mg. per 100 ml. before the test and from 67.0 ± 3.0 to 71.0 ± 2.0 mg. per 100 ml. during the same period that the other subjects smoked. Thus no significant change occurred in the levels of blood sugar during and after the smoking in the group that smoked nor at any time in the control group.

Epinephrine-like Substances (Pressor Amines). Forty-eight determinations of epinephrine-like substances were carried out. Twenty-four were made 4 to 5 minutes prior to smoking, 22 between the third and fifth minutes of smoking and two 1 minute after smoking. Before smoking, the concentrations of epinephrine-like substances ranged from 0.7 to 4.0 μg. per 100 ml. of blood with an average of 2.4 ± 0.2 μg. (table 1). The mean value
maximal observed decrease of the temperature of the toes was 5.7 and the minimal change 0 C. The greatest decrease of the temperature of the fingers as well as of the toes occurred most commonly between 20 and 30 minutes after the smoking was begun. The mean temperature of the fingers decreased 4 C, while that of the toes decreased 1.9 C.

The average change in the skin temperature of the nonsmoking group was as follows: fingers 0.7 and toes 1.1 C.

Blood Pressure. The average basal blood pressure of the 24 subjects was 103 ± 1 mm. Hg systolic and 72 ± 2 mm. diastolic. The systolic pressures ranged from 90 to 120, while the diastolic pressures ranged from 58 to 90 mm. The mean systolic pressure during smoking was 124 ± 2 mm. and the mean diastolic pressure was 88 ± 1 mm. The observed increment in systolic pressure ranged from 10 to 36 mm., and in diastolic pressure from 4 to 30 mm. The maximal systolic pressure occurred after 7.6 minutes of smoking, and the maximal diastolic pressure was observed after 4.5 minutes (fig. 1).

The 3 control studies revealed a mean pressure of 111 ± 2 mm. systolic and 78 ± 2 mm. diastolic, which increased during the time corresponding to smoking of the other subjects to 118 ± 4 systolic and 85 ± 3 mm. diastolic. The greatest change in blood pressure was associated with venipuncture for withdrawal of blood.

Pulse Rate. The mean pulse rate of the 24 individuals was 63 ± 2 beats per minute before smoking. During smoking the mean pulse rate increased to 86 ± 2, while in the 3 control subjects the mean pulse rate of 70 ± 4 before blood was withdrawn rose to 73 ± 5 during and after blood was drawn.

Cold Pressor Test. The mean systolic pressure increased from 108 to 140 mm., while the diastolic pressure rose from 76 to 104 mm. during the cold pressor test. Twenty-two of the volunteers were grouped as vascular hyperreactors; only 2 were called "normal reactors."
EFFECT OF SMOKING ON BLOOD SUGAR

Discussion
The question may arise as to whether our subjects did absorb the nicotine or whether they smoked cigarettes with low nicotine content. However, the significant rise of the pulse rate and blood pressure and the decrease of the skin temperature of the fingers and toes showed definitely a stimulation of the sympathetic nervous system. Indeed, the effect on the blood pressure, pulse rate, and skin temperatures shows a remarkable agreement with those reported previously by one of us.19, 20

The controversy in regard to the elevation of the fasting blood sugar by smoking has continued over a period of years. In an attempt to resolve this question, this investigation was carried out under basal conditions, in a constant temperature room and in a supine position. All possible psychic and physical stimuli were excluded. The venipuncture was carried out before the smoking began and the siliconized needle remained in the vein without another venipuncture, thus avoiding further somatic stimuli. Under these conditions, in contrast to the observations of most other investigators, no increase of the fasting blood sugar was observed during and after smoking. Likewise the smoking of 2 cigarettes with a longer interval of 30 minutes between the smoking of the first and second cigarette did not influence the blood sugar. The epinephrine-like substances in the venous blood also remained unchanged during as well as after smoking. Apparently the amount of secreted epinephrine-like substances in the systemic circulation was not sufficient to raise the total epinephrine-like substances in the blood, as measured with the Weil-Malherbe and Bone method, nor to increase the fasting blood sugar.

Summary
When 24 normal subjects under basal conditions smoked two thirds of 2 cigarettes, there was no appreciable rise in the levels of the fasting blood sugar and the epinephrine-like substances of the systemic venous blood. However, the smoking of two thirds of 2 cigarettes significantly raised the blood pressure and pulse rate, and decreased the skin temperature of fingers and toes. The conclusion may be drawn, therefore, that the smoking of cigarettes is not a likely cause of erroneous diagnosis of diabetes mellitus owing to the elevation of the blood sugar.

Summario in Interlingua
Quando 24 subjectos, sub condiciones basal, fumava duo tertios de 2 cigaretas, nulle appreciabile augmento esseva notate in le nivellos del suero de sanguine in stato jejune del substantias epinephrinoide del sanguine venose sistemic. Tamen, le fumar de duo tertios de 2 cigaretas augemtava significativemente le tension del sanguine e le frequentia del pulso e reduceva le temperatura cutanee in le digitos manual e pedal. Nos pote concluder, per consequente, que le fumar de cigaretas non es un causa probabile de un diagnose erronee de diabete mellite super le base de un elevation non-diabetic del suero del sanguine.

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Various stages in the evolution of the renal lesions of malignant nephrosclerosis were present at necropsy in 100 patients with the clinical diagnosis of severe essential or malignant hypertension. Of the 100 patients, 19 were found to have evidence of "healing" or regression of the acute destructive lesions of malignant nephrosclerosis; all of these 19 patients had been under treatment with potent antihypertensive agents. The most dramatic regression of the lesions occurred in patients under therapy for at least 4 months. The untreated patients possessed vascular changes in the small arteries and arterioles, whereas the treated patients had extensive subintimal fibrosis in the large arteries which, in some instances, had progressed to vascular occlusion. It is the latter lesion which presumably led to the slowly progressing renal failure which was the cause of death in a majority of the treated patients in the group. The hypertensive state is presumed to result in damage to large and medium-sized arteries which may, in part, contribute to the subsequent appearance of atherosclerosis and intimal hyperplasia even though the arterial pressure may be more or less controlled. Lastly, it appears that the acute destructive vascular lesions of malignant nephrosclerosis are caused by increased arterial pressure.

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