tion of the frequency for alternating current, then the potential difference across this element should build up as a power function of the time after a constant current is started through it. The strength of current necessary to change the potential by a fixed value e_0 in the time t is then given by $i = i_1 t^{-\alpha}(2)$, where $i_1 = e_0 \Gamma (1+\alpha)/z_1$.

It is reasonable to assume that this polarization element is to be identified with the cell membrane and that a threshold change of potential across the membrane will stimulate an excitable tissue. When it is further assumed that the membrane parameters are constant up to a threshold potential change, then the strength-duration relation for constant current excitation should be given for short times by equation (2).

The fixed resistances of the equivalent tissue circuit may be neglected for stimuli of short duration, but they are important for the longer stimuli and determine the rheobase. In the general case, the superposition[4] formulation and the Heaviside operational method lead to the same asymptotic expansion for e(t). For the simple condenser hypothesis, $\alpha = 1.0$ and the solution is well known. The Nernst diffusion hypothesis corresponds to $\alpha = 0.5$ and the solution may be given in terms of the error function.[5] This theoretical membrane potential change has the general form of the subthreshold direct current excitability curve[6] up to its maximum, but does not give the subsequent decrease, which is found experimentally.

Both alternating current conductance and direct current excitation data on the same preparation are not yet available, but equation (2) has at least qualitative support. Conductance measurements show that the polarization elements often have an approximately constant phase angle for the complete frequency range or at least a major portion of it.[7] Equation (1) gives a value of α from 0.62 to 0.71 for frog sciatic nerve,[8] and 0.73,[7] 0.79[9] for mammalian muscles. Excitation data for short times give a value of α from 0.53 to 0.86 for frog and toad sciatic,[10] and 0.75 for toad sartorius muscle.[11] These data suggest that conductance and excitation phenomena involve the same polarization element and that this element is not represented by either the condenser or Nernst hypotheses in their simple forms.

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[4] The author is very much indebted to Professor H. T. Davis, of Indiana University, for the inversion and expansion of the Volterra integral equation encountered.

[5] Campbell and Foster, *loc. cit.*, Pair No. 551.

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THE EFFECTS OF CIGARETTE SMOKING UPON THE BLOOD SUGAR[1]

THE gratification derived from smoking has always been rather a mystery. Exactly what elements in the smoke exert the pleasurable physiological effects has never been determined, nor precisely what these effects are. Numerous theories have been advanced. But these theories merely show how little is known.

Tobacco differs from other leafy vegetables in its characteristic alkaloid. That alkaloid, nicotine, is named for Jean Nicot, who introduced tobacco chewing to Catherine de Medici. Nicotine is a powerful drug. It paralyzes nerve ganglia when applied directly to them. But it has not been shown—and it is on the whole improbable—that this property of nicotine accounts for the effects of tobacco smoking.

Chemists have pointed to the carbon monoxide in tobacco smoke and have suggested that it is a cause of the ill effects, if not the pleasure, of smoking. But in fact a heavy smoker accumulates less carbon monoxide than does the non-smoker who takes a walk on Fifth Avenue, New York, during the hours of heavy automobile traffic.

Other products of combustion, notably pyridine, have likewise been suggested; but they occur, not only in tobacco smoke, but also in the smoke from other vegetable matter, such as corn silk, maple leaves and coffee beans. That these substances do not contribute appreciably to the gratification of smoking is conclusively demonstrated by the fact that few smokers adhere to the juvenile substitutes for tobacco. Such substitutes are cheap, yet tobacco maintains its popularity. Why tobacco?

The answer we believe is nicotine. Smoking, we find, produces a definite, although temporary, increase in the concentration of blood sugar, and a corresponding increase in the rate of sugar combustion in the body. These effects certainly are due to the nicotine of the tobacco and they arise from the action of this alkaloid upon the adrenal glands. There can be little doubt that this is the source of at least a considerable part of the gratification from smoking.

Our observation of the hyperglycemia from smoking occurred by chance. We had been investigating the question of the optimum mealtime interval—how often should children, college students and industrial workers be fed. To this end we determined the respiratory quotients, at hourly intervals during the day, on several hundred subjects. In a number of cases

[1] From the Laboratory of Applied Physiology, Yale University.

the concentration of sugar in the arterial blood was compared with the respiratory quotient.

On some days the subjects fasted; on others they ate from one to five meals, variously spaced. As was to be expected, the respiratory quotients of the fasting subjects fell to values between .78 and .82 and the blood sugar to .08 and .10 per cent. In the subjects who ate, both the respiratory quotient and the blood sugar rose after the meal; but within 2 to 4 hours, if another meal was not taken, it fell again to the fasting level. When this fasting level was reached, it was maintained in the great majority of the subjects with little change for many hours. A few, however, exhibited sudden fluctuations of considerable magnitude in both the respiratory quotient and blood sugar.

Such fluctuations never occurred among the children. All the adults were free from emotional disturbances which might explain them. A search for the cause of the divergent values suggested that it was associated with smoking.

The respiratory quotients and blood sugars before and after smoking were then studied in a number of subjects. The results showed that when the respiratory quotient is above .85 and the blood sugar correspondingly above .13 per cent., the smoking of a cigarette has no appreciable influence upon either. When, however, the respiratory quotient and blood sugar have fallen below these values, and especially when the fasting level has been reached, the smoking of a cigarette is followed by a rise in both. Values are attained within 15 minutes as high as .85 or .90 for the respiratory quotient and .12 or .14 per cent. for the sugar. During the next 30 minutes the values fall gradually to, or slightly below, those observed before the cigarette was smoked.

It is a well-known fact that injection of nicotine into animals is followed by a temporary rise in blood sugar.[2,3,4] But so far as we can find no one has previously reported a similar rise in man resulting from the nicotine of tobacco smoke.

From animal experimentation it is well established that it is the action of nicotine upon the adrenal glands which leads to the hyperglycemia.[3, 5, 6, 7] The rate of discharge of adrenalin is increased; and the liberated adrenalin exerts its characteristic glycolytic action. The glycogen stored in the liver and muscles is converted into sugar. In consequence the concentration of sugar in the blood is increased. Secondary to the rise in sugar the combustion of carbohydrate is increased and can be observed in the increase in the value of the respiratory quotient. But, as already stated, these metabolic effects do not result from smoking when the blood sugar is at a concentration above .13 per cent. as it is for 2 to 3 hours following a meal.

The acceleration of sugar metabolism thus demonstrated affords a possible explanation for the fact that smoking diminishes hunger in many users of tobacco. Hunger appears from our observations and those of other investigators to arise within a definite time after the blood sugar falls to the fasting level. Tobacco smoking, by inducing a hyperglycemia, may thus delay temporarily the development of hunger.

Our observations on the mealtime intervals indicate that the hyperglycemia following a meal definitely relieves the fatigue and irritability that generally develop soon after the fasting level of blood sugar is reached. Smoking by inducing a hyperglycemia temporarily relieves these conditions.

The other effects of smoking, the acceleration of the pulse and the temporary rise in arterial pressure, are presumably, like the increase in sugar concentration, dependent upon discharge of adrenalin.

Our observations demonstrate why tobacco rather than any other substance is used for smoking; the smoker obtains from tobacco repeated minute doses of nicotine.

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