Physiological Effects of Smoking

By J. M. WALKER, *Department of Pharmacology, University of Oxford*

An enormous amount has been written about the effects of smoking, some of it difficult to assess, because evidence about smoking is often subjective and because some writers have obviously been influenced in their interpretation of results by a strong dislike of the habit. However, there remains much of interest and importance. Most of this deals with acute effects on the body of smoking and especially of nicotine; where workers have studied its actions over long periods, they have been interested primarily in the production of pathological states, such as coronary disease and carcinoma of the lung. There is thus comparatively little experimental work on the effect of habitual smoking on nutrition, and much of what I shall have to say will be conjecture.

Effect on body-weight

It is a common clinical observation that some middle-aged persons who suddenly stop smoking rapidly gain in weight. Koehler, Hill & Marsh (1947) studied this phenomenon in patients suffering from malnutrition. They had formed the impression that excessive smoking caused in their subjects a failure to gain body-weight as they should and that if they stopped smoking their nutritional state was quickly improved. To test this, they selected six patients, each of whom was smoking regularly fifteen to thirty cigarettes a day. Their body-weights had reached a steady level that was considered to be too low. They were told to stop smoking and observed for periods varying from 8 to 36 weeks. Every one of them at once began to put on weight, the amount gained per week being between 0·5 and 1·6 lb., with a mean of 1·1 lb. The authors do not say whether they observed at the same time a control group of smokers, nor is it clear how long their subjects remained at a steady level of weight before being put to the test of not smoking. Nevertheless, these results give support to the idea that there is a connexion between smoking and nutrition.

Increase in body-weight could be caused in several ways. Apart from any effects on water metabolism, which will be discussed later, it could be due to decreased metabolic rate, a lower level of bodily activity, an increased absorbtion from the gastro-intestinal tract, an increased food intake or a combination of two or more of these factors. About the first three there is little to be said, though they cannot be entirely excluded. Smoking does increase the basal metabolic rate a little in some subjects (Dill, Edwards & Forbes, 1934), probably by liberating adrenaline, but its action is slight and transient. There is no evidence that it increases bodily activity and that those who give it up become more torpid; indeed my own impression is that the opposite is true. It is not possible to say what effect, if any, smoking has on the assimilation of food; it certainly has no important influence on gastric secretion and gastric emptying (Schnedorf & Ivy, 1939), and Koehler

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et al. (1947) reported that the enzyme activity of the intestinal juices of smokers and non-smokers was the same. We are left ,therefore, with an increased food intake as the most likely cause of the gain in weight, and this idea is supported by the observation that many of these people develop an enhanced appetite.

The problem is to find out what it is in tobacco that lessens the appetite and how it does so. Possibly the very act of putting a pipe or cigarette in the mouth is partly responsible, and there may be other factors, such as a derangement of the faculties of taste and smell. But if there is a pharmacological effect, nicotine may well be the responsible substance.

Effect on hunger contractions. Carlson & Lewis (1914) showed that smoking depressed or abolished the movements of the stomach known as hunger contractions. How it does this is not clear. They thought that it was a reflex action depending on stimulation of nerve endings in the mouth. Another possibility is that the nicotine absorbed liberates adrenaline, which is known to inhibit gastric movement. The adrenaline may do this by raising the blood sugar, though efforts to show that the intravenous injection of glucose abolishes these contractions have led to conflicting and mainly negative results (Quigley & Hallaran, 1931, 1932). However that may be, the control of food intake is now no longer thought to repose in so lowly an organ as the stomach. It has been shown, for instance in dogs, that injection of insulin causes marked hunger contractions and an increased intake of food. But when the vagi are cut in these animals and the contractions thereby abolished, the increased food intake after insulin persists (Grossman, Cummins & Ivy, 1947). It seems likely that appetite depends on the blood-sugar level apart from sensations of hunger due to movements of the stomach. Does smoking affect the blood sugar?

Effect on blood sugar. Lundberg & Thyselius-Lundberg (1931) showed that smoking caused a rise of the blood sugar to a value about 50% above the resting level, to be succeeded by a gradual fall to normal in about half-an-hour; this action was not seen when nicotine-free cigarettes were smoked. Haggard & Greenberg (1934) observed the same effect, but found that it was not present in those of their subjects whose blood-sugar level started at or above 130 mg /100 ml. The effects on the blood sugar and the subject's sensations seem to be closely correlated. Thus Wachholder (1948) found that his subjects varied. In most of them the blood sugar rose and hunger was abolished. In a few, the blood sugar fell, and in these hunger was provoked or, if already present, was made more severe. Again, the most likely explanation of the rise is that nicotine liberated adrenaline, for Short & Johnson (1939) found that injections of adrenaline could be made to imitate closely the effects of smoking on the blood sugar and indeed on the cardiovascular system generally.

Effect on the hypothalamus. I want to suggest a third mechanism, namely that tobacco acts directly or indirectly on the hypothalamus. Consider amphetamine, which is very effective in reducing appetite. Little is known about its mode of action. It certainly inhibits gastric contractions in dogs when given in large doses, but it is also effective in amounts too small to affect the stomach and in animals whose

stomachs are completely denervated (Sangster, Grossman & Ivy, 1948). It does not raise the blood sugar. It seems reasonable, then, to suppose that it, and nicotine like it, acts on the brain. Williams, Doughaday, Rogers, Asper & Towery (1948) studied a number of compounds that reduced the appetite. If we add to their list cocaine (Grossman & Cummins, 1947) and, tentatively, nicotine, we find that all the substances shown in Table 1 have two properties in common. First, they are all stimulants of the central nervous system. Secondly, they are sympathomimetic,

Table 1. *Compounds causing loss of appetite*

D–Amphetamine (Dexedrine)	Williams *et al.* (1948)
1–Cyclohexyl-2-aminopropane	
1–Cyclohexyl-2-methylaminopropane	
Methylamphetamine (Methedrine)	
2–Amino-6-methylheptane	
DL–Amphetamine (Benzedrine)	
1–(*p*-hydroxyphenyl)-2-aminopropane (paredrine)	
l–Amphetamine	
Cocaine	Grossman & Cummins (1947).
? Nicotine	?

nicotine because it liberates adrenaline, the other compounds because they inhibit the action of amine oxidase and thus protect adrenaline from destruction. It would be interesting to know whether these properties are important in producing their anorexigenic action.

Effect on water metabolism

Antidiuretic effect. It is well established that, under experimental conditions, cigarette smoking inhibits water diuresis in man (for review, see Burn, 1951). The intravenous injection of an appropriate amount of nicotine has the same effect, and there is good evidence that its action is due to the liberation of the antidiuretic hormone from the neurohypophysis. From the nutritional point of view, the implications of this are not clear. Habitual smokers appear to be more tolerant to the action than non-smokers, and this fact may lessen its importance. A few smokers have told me that on giving up the habit they became aware of an increased excretion of urine, but I do not know whether or not it is a common observation that those who abandon smoking increase their output of water as well as their intake of food.

Diuretic effect. Nicotine temporarily inhibits water diuresis in rats as it does in man. But, although after nicotine the time taken to reach a maximum rate of excretion is prolonged, the total volume of urine passed is increased. This fact has emerged by chance from some work in which Dr. G. W. Bisset and I were investigating the effect of the ganglion-blocking agent hexamethonium on the antidiuretic action of nicotine. Table 2 gives the mean total amounts of urine excreted by groups of four rats, after each rat had received by stomach tube 5 ml. water per 100 g body-weight. There is no difference in the amounts excreted by rats receiving hexamethonium and by those receiving no drugs. Similarly, there is no difference

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Table 2. *Amounts of urine excreted by rats given by stomach tube 5 ml. water/100 g body-weight. Each figure is the mean volume of urine in ml. excreted by four rats*

Drug	Volume				Mean
Nicotine with hexamethonium	35·9	42·1	44·6	42·2	41·2
Nicotine alone	38·1	39·4	47·7		41·7
Hexamethonium alone	33·2	29·9	38·6		33·9
No drug	30·1	33·1			31·6

between the groups receiving nicotine and hexamethonium and those receiving nicotine alone. But the mean volumes excreted by rats receiving nicotine are much greater than those of the groups receiving none. We do not yet know how this diuresis is brought about, nor whether it has any significance for smokers. The amounts of nicotine given to the rats (0.5–1·0 mg nicotine acid tartrate per 100 g body-weight) were relatively enormous compared with what would be absorbed by a man who smoked, and I know of no evidence that smoking ever causes a diuresis.

We have considered two aspects of the physiological effects of smoking. The effect on body-weight is of practical importance but not clearly understood; that on water metabolism is clearly established experimentally, but of doubtful significance.

REFERENCES

Burn, J. H. (1951). *Brit. med. J.* ii, 199.
Carlson, A. J. & Lewis, J. H. (1914). *Amer. J. Physiol.* **34**, 149.
Dill, D. B., Edwards, H. T. & Forbes, W. H. (1934). *Amer. J. Physiol.* **109**, 118.
Grossman, M. I. & Cummins, G. M. (1947). Quoted by Harris, S. C., Ivy, A. C. & Searle, L. M. (1947). *J. Amer. med. Ass.* **134**, 1468.
Grossman, M. I., Cummins, G. M. & Ivy, A. C. (1947). *Amer. J. Physiol.* **149**, 100.
Haggard, H. W. & Greenberg, L. A. (1934). *Science*, **79**, 165.
Koehler, A. E., Hill, E. & Marsh, N. (1947). *Gastroenterology*, **8**, 208.
Lundberg, E. & Thyselius-Lundberg, S. (1931). *Acta med. scand.* Suppl. 38.
Quigley, J. P. & Hallaran, W. R. (1931). *Amer. J. Physiol.* **97**, 552.
Quigley, J. P. & Hallaran, W. R. (1932). *Amer. J. Physiol.* **100**, 102.
Sangster, W., Grossman, M. I. & Ivy, A. C. (1948). *Amer. J. Physiol.* **153**, 259.
Schnedorf, J. G. & Ivy, A. C. (1939). *J. Amer. med. Ass.* **112**, 898.
Short, J. J. & Johnson, H. T. (1939). *J. Lab. clin. Med.* **24**, 590.
Wachholder, K. (1948). *Arch. exp. Path. Pharmak.* **205**, 115.
Williams, R. H., Doughaday, W. H., Rogers, W. F., Asper, S. P. & Towery, B. Y. (1948). *Ann. intern. Med.* **29**, 510.

The Effect of Lesions in the Hypothalamus on Appetite

By G. C. KENNEDY, *Clinical Endocrinology Research Unit, Royal Infirmary, Edinburgh*

In the light of knowledge acquired in the last few years, it now seems natural to think of the hypothalamus and the pituitary as almost inseparable parts of functional unit. The pituitary is anatomically conspicuous, its main structural features being obvious even to the naked eye; the structure of the hypothalamus remains something of a mystery in spite of present-day microscopical techniques. The pituitary