

TOBACCO

Experimental and Clinical Studies

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SUPPLEMENT III

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spoils the taste of smoking (Arvidsson, 1971). And, in one control treatment of smoking reduction devised by Marston and McFall (1971), subjects used a pill designed to coat the mouth to make cigarettes aversive [see above, 1145 for details].

Presumably, inducing the smoker to *over-smoke*, thus adding nicotine upon nicotine, would spoil his smoking pleasure and thus reinforce his decision to stop smoking [((308))]. Experimentally, Jervik, Glick and Nakamura (1970) investigated inhibition of cigarette-smoking by orally-administered nicotine [for experimental details, see above, 1131]. The subjects—all habitual smokers—self-administered 5 nicotine pills at intervals on each of 4 consecutive days, and such ingestion produced a small but significant decrease in the number of cigarettes smoked. To demonstrate essentially the same point, Frith (1971b) investigated the effect of varying the nicotine content of cigarettes on smoking behavior, and found that cigarettes of all types produced a decrease in the desire for a cigarette immediately after they had been smoked, but the size of this decrease varied directly with the nicotine content. A linear relationship between nicotine content and time to smoke a single cigarette was found, such that the more nicotine there was in a cigarette, the longer a subject took to smoke it [see above, 1131].

The wide-spread use of lobeline preparations in the treatment of the smoking habit is a form of "substitution therapy", in which lobeline (which has a weak nicotine-like action) substitutes, as it were, for nicotine during the first (pharmacological) phase of tobacco dishabituation, after which lobeline itself is discontinued without withdrawal syndrome [((308))]. Anti-nicotine preparations with a lobeline base include Banton, Lobidan, and Tabusine, which are said to be not habit-forming and to act on the respiratory system, and replace nicotine present in the tissues of the smoker, so the lack of nicotine is not perceived (Bridel, 1970). In their smoking-control program [described above, 1145-B. *United States*], Jacobs and associates (1971) administered lobeline to one group of subjects, and reported that treatment without drugs was more effective than taking medication, especially for high-risk cases. A. Rosenberg (1970) expressed a preference for mental approaches over lobeline in weaning smokers from their habit; and Markiewicz (1971b) advocated that lobeline administration should be accompanied by psychiatric treatment. In such a combination therapy, 250 heavy smokers were treated from 2 to 4 weeks; and altogether, 70% of these showed partial or complete abstinence (Markiewicz, 1971b). Other drugs were not as effective. For instance, of 23 patients treated from 4 to 8 weeks with Atarax [Hydroxyzine HCl], only 1 ceased smoking. This writer also stated that amphetamine, given in doses of 10 mg, can bring about a lowering of the tobacco intake by 50%; but he concluded that smoking can be reliably stopped only if orders issued to this effect are rigidly enforced.

Bacarov [(1967) ((247))] presented results of tests with Tabex, a Bulgarian anti-smoking preparation, the active principle of which is cytisine, an alkaloid from *Cytisus laburnum*, said to have a lobeline-like effect. Benndorf, Scharfenberg and associates (1970) reported the results of a 6-month investigation of participants who had voluntarily engaged in smoking-withdrawal treatment. Inquiry was made of 395 persons as to whether they had again commenced smoking 4 weeks after a detoxification treatment with Tabex. Only 204 persons returned the mailed question-

naire, of whom 23.5% had abstained from smoking at the time of the inquiry. Subsequently, Scharfenberg, Benndorf and Kempe (1971) conducted a double-blind test of the dehabituating effects of Tabex. Of 66% who could be evaluated 2 years following administration of the drug, 47% of the patients treated with Tabex were still non-smokers. Compared to the results achieved by means of only a placebo, the difference was statistically significant, and Tabex was therefore recommended as a medical aid for cessation of smoking. [In these papers by Benndorf and Scharfenberg and associates, Tabex is described as containing cytosine.] Paun and Franze (1969), reporting on 20 smokers who wanted to abandon the habit, undertook the withdrawal of tobacco in group therapy with a cytosine-containing preparation. The results obtained were said to be superior to those from a placebo; 35% of the patients were no longer smoking after 4 weeks, and 46% were no longer smoking after one-half year.

In their investigation of inhibition by drugs of smoking behavior in monkeys [described above, 1125], Glick, Jervik and Nakamura (1970) found that both scopolamine and amphetamine reversed the tobacco-smoke-air preferences of their experimental animals, and over-all puffing rates were greatly decreased; subsequent tests indicated that increased thirst caused by these drugs may have made smoke more aversive. The authors warned that these findings must be qualified because of their questionable correspondence to human smoking, and that their ultimate importance will depend on their therapeutic significance in their smoking-control program [described above, 1145-B. *United States*], Jacobs and colleagues (1971) employed amphetamine as one of the drug conditions, and found that treatment without drugs was more effective than taking medication, especially for high-risk cases. When given doses of 5 and 10 mg *d*-amphetamine, the subjects in an experiment reported by Schuster (1970, p. 193) increased their cigarette-smoking frequency by about 25%. This increased smoking, however, was said to be probably a result of a non-specific stimulant effect of the drug, since the subjects were observed to be more loquacious and active.

At a smoking-withdrawal clinic at Lund Hospital, Lund, Sweden, 191 men and 99 women were treated in the course of one year by s.c. injections of 0.125 mg methyiscopolamine once a day for at least 2 weeks, and additional injections every other day or every third day for the following 2 weeks. Scopolamine was also administered orally, 2 tablets 2 or 3 times daily, but without effect. In all, 36 (19%) men and 12 (12%) women were free of smoking one year after having completed the cure. The results, although considered to be disappointing, were noted by the reporter, Wetterqvist (1971), to correspond well with other smoking-withdrawal experiences in Sweden and abroad.

J. W. Evans (1971) reported that 40 patients (20 men and 20 women) took part in a double-blind cross-over trial designed to compare the possible effects of fenfluramine with that of a placebo as an aid to stopping smoking. The results showed that fenfluramine was no more active than the placebo in removing the desire to smoke cigarettes. The patients were highly motivated and had volunteered to take part in the study, rather than being told by their physician that they must stop smoking. In spite of this, less than a third of them (12) could complete the trial. The group of patients who dropped out contained at least 12 who did initially reduce their cigarette consumption, and these were more numerous (9 out of 12) among those