Temperature Profiles Throughout Cigarettes, Cigars, and Pipes

The recent interest in a correlation between cigarette smoking and cancer, such as the isolation of carcinogens from cigarette paper, prompts me to offer some evidence I obtained on this subject. During a lull in some work I was doing at the Whiting Laboratories of Standard Oil (Indiana), I had a high-speed, high-temperature Micromax recorder at my disposal, which I used to measure the temperature profiles throughout cigarettes, cigars, and pipes. Since I have never found any mention of these temperatures, I believe that other readers may be interested in them. I found as much as a 300°C difference between the "hot spots" in a cigarette and those in a pipe. Most moderately priced cigars had "hot spots" approaching that of cigarettes.

The temperature profile throughout the burning tobacco was measured by the insertion of six glass-coated 28-gage chromel-alumel thermocouples throughout the tobacco bed. The temperature-time curves were then recorded on the Micromax recorder as the tobacco was smoked. In this way, as the "hot spot" approached a given thermocouple its temperature rapidly rose and then dropped as the "hot spot" passed. The over-all burning temperature was then considered to be the average of the maximum temperature reached by all six thermocouples. The six maximum temperatures so measured were all within 10°C of one another.

The popular brands of cigarettes had "hot spots" that varied between 610°C and 740°C, depending on the brand. The temperature of the gases entering the mouth varied from 50°C to 70°C, also depending on the brand of cigarette. The temperature-time curves were smooth curves showing no discontinuity.

Repetition of this same procedure with low-priced cigars showed the same maximum temperature range of the "hot spot," from 600°C to 660°C, with the gases entering the mouth at 40°C to 60°C. More expensive cigars showed maximum temperatures from 580° to 610°C.

Highly aromatic pipe tobacco showed a maximum temperature of 540°C to 590°C, while untreated, nonaromatic tobaccos showed a "hot spot" in the pipe of only 420°C to 450°C. The temperature of the gases at the bottom of the pipe bowl at the entrance to the stem was as low as 30°C with some tobaccos and ranged up to 50°C. However, in all tobaccos examined, the temperature of the gases from pipe tobacco was lower than that of the gases from a cigarette. I believe that the wide difference in aromatic and nonaromatic pipe tobacco and the wide temperature difference between cigarettes and pipes must be due, in part, to the potassium chlorate used to treat cigarette tobacco in order to insure even and continued burning. The aromatic odorant used to treat aromatic pipe tobacco may be responsible for the increased temperature of the "hot spot" found in aromatic pipe tobaccos.

Having thus established the temperature range in the "reaction zone" in tobacco, one might conclude that the carcinogenicity of cigarettes over pipe tobacco is due to the 300°C higher temperature found in cigarettes. However, most cigars also show the 600°C "hot spot," and recent evidence would tend to indicate that cigars are not carcinogenic. Since the 600°C temperature range in cigarettes is more than sufficient to decarboxylate or decarbonylate pyridine or pyran carboxylic acids or aldehydes, it would seem possible, from a chemical viewpoint, that the carcinogenic pyrans and pyridines arise from the cigarette paper. Furthermore, in view of the extreme high temperatures in cigarettes, thermal cracking to yield free radicals which could subsequently dehydrocyclize to yield condensed ring carcinogens is not an unreasonable postulate.

CHARLES R. GREENE
49 Norwood Avenue, Berkeley, California

31 December 1954

Aureomycin in the Saliva of Dairy Calves after Intramuscular Injection of the Antibiotic

In a preceding study, Radisson (*1*) showed that during continuous feeding of terramycin to dairy calves, high concentration of the antibiotic could be detected in both feces and urine. Rusoff *et al.* (*2*) reported that Aureomycin (*3*), following either oral administration or intramuscular injection, also could be detected in both of these forms of excreta. Since growth stimulation was obtained whether Aureomycin was given orally or intramuscularly, the latter authors assumed that injected Aureomycin "by-passed" the rumen and concluded: "The mode of action of Aureomycin in stimulating growth in the young calf is not due to its action in the rumen." In view of the evidence presented by Bender *et al.* (*4*) that saliva from human beings who had been injected intravenously with Aureomycin contained significant quantities of this antibiotic, an attempt was made to determine whether the same might occur in the young calf (*5*).

In preliminary work attempts were made to detect Aureomycin in the saliva of several calves after intramuscular injection of the antibiotic. The standard paper-disk method for assay of antibiotics was used, with spores of *B. subtilis* (ATCC No. 6633, DIFCO) as the test organism; considerable difficulty was experienced in consistently detecting small quantities of Aureomycin in the saliva. But, when the cup-plate method was used, with spores of *B. mycoides* (*6*) as the test organism, and when the saliva sample was adjusted to *p*H 6.5, it was possible to detect Aureomycin concentrations as low as 0.05 μg/ml.

The results reported here (Table 1) involved four ruminating calves, 7 to 9 weeks of age, that consumed 2 to 5 lb of a grain mixture, plus hay, daily. A single dose of 2 g of Aureomycin HCl in sesame oil was injected intramuscularly (in the semitendinosus of the hind leg) into each calf immediately after the morning feeding. Samples of saliva, approximately 15 ml each, were collected at intervals of 0.5, 1, 2, 3, 5, 8, 12, and 24 hours after injection of the antibiotic. The samples were stored immediately in a freezer and kept frozen until completion of all the collections from each calf. Standard curves were prepared by plotting the size of the zones of inhibition produced by known quantities of Aureomycin added to saliva, which had been obtained from calves receiving no Aureomycin, and which also had been adjusted to *p*H 6.5.

As early as ½ hour after intramuscular injection of Aureomycin, the antibiotic was detected in the saliva of three of the four calves (Table 1). From 2 to 8 hours after injection, with one exception, Aureomycin was present in the saliva of all four calves at all collections. At 12 hours, the antibiotic was still detected in

Table 1. Concentration of Aureomycin found in the saliva of dairy calves following intramuscular injection of the antibiotic

Calf No.	Breed	Weight (lb.)	Concentration of Aureomycin in saliva (μg/ml)							
			Hours after injection							
			0.5	1	2	3	5	8	12	24
1	Jersey	90	0.25	0.35	0.15	0.00	0.05	0.10	0.10	0.00
2	Jersey	101	0.00	0.00	0.10	0.20	0.15	0.20	0.00	0.00
3	Guernsey	130	0.05	0.05	0.10	0.25	0.05	0.05	0.00	0.00
4	Ayrshire	115	0.10	0.20	0.25	0.20	0.10	0.10	0.10	0.00

the saliva of two of the calves, but after 24 hours none of the antibiotic was found in any of the calves.

Since the Aureomycin was found in the saliva, some of the antibiotic would necessarily pass into the rumen and consequently might have some effect on the rumen microflora. The effects of antibiotics on rumen microflora and on efficiency of digestion *in vitro* and *in vivo* have been studied, and reports are in preparation. In the continuation of the work of Rusoff *et al.* (*2*), it was reported by Hester *et al.* (*7*) that Aureomycin could not be detected in the rumen following intramuscular injection of Aureomycin. It is possible that the failure of the latter authors to detect Aureomycin in the rumen contents of slaughtered animals might be ascribed to the considerable dilution of saliva after it passes into the rumen, to the smaller amounts of Aureomycin injected, to a possibly less sensitive assay technique than that described in the saliva analyses reported here, or to a combination of all three factors.

J. J. RADISSON*
E. E. BARTLEY
F. C. FOUNTAINE
F. W. ATKESON

Department of Dairy Husbandry, Kansas Agricultural Experiment Station, Manhattan

References and Notes

1. J. J. Radisson, thesis, Michigan State College (1952).
2. L. L. Rusoff *et al.*, *J. Dairy Sci.* 37, 488 (1954).
3. Aureomycin is the trademark of Lederle Laboratories Div., American Cyanamid Co., for the antibiotic chlortetracycline. The Aureomycin used in these experiments was obtained through the courtesy of R. F. Elliott, Lederle Laboratories.
4. I. B. Bender, R. S. Pressman, S. G. Tashman, *J. Dental Research* 32, 435 (1953).
5. This paper is contribution No. 234, Department of Dairy Husbandry, Kansas Agricultural Experiment Station. This work was supported in part by a grant from Lederle Laboratories.
6. Culture of *B. mycoides* was obtained through the courtesy of H. P. Broquist, Lederle Laboratories.
7. H. H. Hester, F. T. Landagora, L. L. Rusoff, *J. Animal Sci.* 13, 988 (1954).

* Present address: Villeneuve, Ain, France.

14 March 1955

Methylpentynol (Oblivon) in the Treatment of Epilepsy

In 1952 R. W. Schaffarzick and B. J. Brown [*Science* **116**, 663 (1952)] published reports of experimental and clinical trials that suggested that methylpentynol might be of use in the treatment of epilepsy. They also noticed that two of the six patients under treatment developed strongly positive cephalin flocculation tests, which rapidly became negative when the drug was discontinued, suggesting that this drug might have toxic effects on the liver. As a result of this report the effect of methylpentynol on patients with epilepsy was further investigated and the effect of the drug on liver function tests was observed.

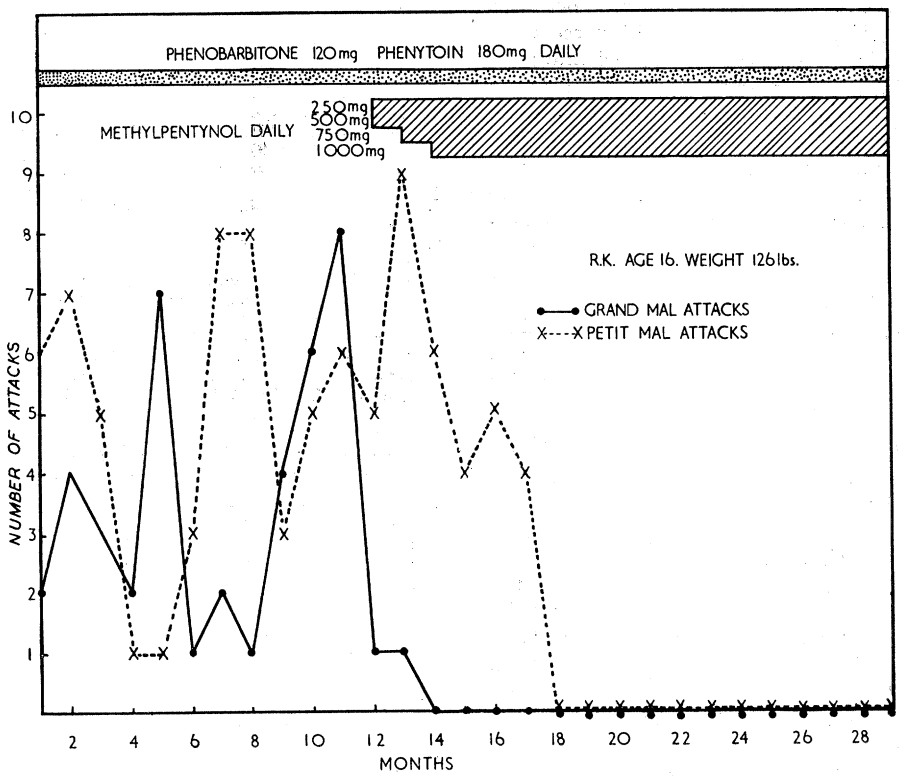

Fig. 1. Effect on epileptic patients of treatment with methylpentynol.

Six children of ages between 11 and 16 years and 18 adult males were treated. All but one of the patients had both grand and petit mal; five had, in addition, psychomotor attacks; the remaining one had psychomotor epilepsy only. Methylpentynol was given by mouth, the dosage being increased up to 1000 mg daily, and treatment was continued for 3 months. In only one patient, a boy of 16, did methylpentynol appear to control the epilepsy; the number of attacks and effect of treatment are shown in Fig. 1. He has now been under treatment with methylpentynol for a further 9 months as an outpatient and has had no further fits. Full empirical liver function tests were performed on all the children at regular intervals up to 3 months and on 10 of the adults at the end of 3 months. No abnormality was found.

Two of the children became sleepy and depressed while they were under treatment; they were inclined to stagger and fall easily. When the drug was omitted they rapidly regained their former wakefulness and spirits.

It is concluded that methylpentynol is unlikely to be useful in controlling epilepsy in patients who have proved resistant to the more usual form of treatment, but that it has no toxic effects on the liver, as far as these tests have shown.

D. G. KENNEDY
J. R. TROUNCE

Lingfield Epileptic Colony and *Departments of Medicine* and *Pharmacology, Guy's Hospital, London*

6 January 1955

γ-Sitosteryl Glycoside in Tobacco

The Indian Cancer Research Centre has been interested for the last 10 years in determining the role of tobacco in the production of oral cancer (*1*). With this object in view, a detailed study of the chemistry of tobaccos that are used for chewing purposes by the people of India has been in progress for the last 2 years. One of the varieties of tobacco extensively used for chewing by the people living in Malabar (southwest coast of India) is known as "Vadakkan" (*Nicotiana tabacum*).

We have now found that it contains a sterol glycoside (I) not so far isolated from tobacco. The glycoside (I) is insoluble in water, sparingly soluble in nonhydroxylic solvents, and crystallizes from alcohol in colorless plates, mp 215°–235°C (found: C, 72.1; H, 10.4; calcd. for $C_{35}H_{60}O_6$: C, 72.8; H, 10.5 percent). Yield 0.01 to 0.02 percent. It yields tetraacetyl derivative, crystallizing from dilute alcohol in lustrous plates, mp 149°C