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# Tar, CO and $\Delta^9$THC Delivery From the 1st and 2nd Halves of a Marijuana Cigarette

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TASHKIN, D. P., F. GLIEDERER, J. ROSE, P. CHANG, K. K. HUI, J. L. YU AND T.-C. WU. *Tar, CO and $\Delta^9$THC delivery from the 1st and 2nd halves of a marijuana cigarette.* PHARMACOL BIOCHEM BEHAV **40**(3) 657–661, 1991.—Previous in vitro studies suggest that, with successive puffs from a marijuana cigarette, delta-9-THC becomes concentrated in the remaining uncombusted portion of the cigarette. These observations are consistent with the common practice of smoking marijuana cigarettes to a smaller butt length than that to which tobacco cigarettes are smoked. The purpose of the present study was to compare the delivery of delta-9-THC, as well as total insoluble smoke particulates (tar) and carbon monoxide, from the distal ("first") versus the proximal ("second") halves of a standard marijuana cigarette during "natural" smoking of marijuana. On 4 separate days, ten habitual marijuana users smoked nearly all or approximately ½ of a standard marijuana cigarette (83 mm length; 800–900 mg; 1.24% THC), as follows: day 1, "whole" cigarette (60 mm smoked, leaving a 23-mm butt); day 2, "first" half (first 30 mm); day 3, "second" half (second 30 mm) after the "first" half was presmoked with a syringe; and day 4, "second" half after the "first" half was excised. A previously described smoking apparatus (20) was used for measurement of puff volume and inhaled tar. Puff volume and number were allowed to vary spontaneously (provided that the specified length of cigarette was consumed), while inhaled volume (1.5 liters), breathholding time (14 s) and interpuff interval (30 s) were held constant. Blood samples were withdrawn prior to smoking and serially after completion of smoking for analysis of blood carboxyhemoglobin (COHb) and serum delta-9-THC. Heart rate was measured before and 5 min after smoking. Subjects rated their level of "high" 20 min after completion of smoking. Compared to the distal half, smoking the proximal half of a marijuana cigarette delivered more tar, carbon monoxide and THC to the smoker's lungs, as indicated by a greater amount of inhaled tar and a larger boost in both blood carboxyhemoglobin and serum THC. In addition, boosts in blood COHb and serum THC were significantly greater following smoking the proximal half after the distal half had been presmoked rather than excised. These findings are probably due to 1) less rod filtration of insoluble particulates, 2) increased concentration in the proximal half of the cigarette of carbonaceous material and THC volatilized by prior combustion of the distal half, and 3) possible differences in burn rate due to effects of precombustion of the distal half on moisture content of the proximal half. Clinical implications of these findings are that smoking fewer marijuana cigarettes down to a shorter butt length to deliver more THC and achieve a greater "high" is potentially more harmful to cardiorespiratory health than consuming a comparable amount of marijuana contained in more cigarettes smoked to a longer butt length.

Marijuana $\Delta^9$-Tetrahydrocannabinol Tar Carbon monoxide "High" Butt length

TWO recent studies conducted in man under natural conditions of smoking have shown that puff volume diminishes during the smoking of the second half of a marijuana cigarette (7,21). Previous in vitro studies demonstrated that with successive puffs from a cigarette, various smoke components, including tar condensate, nicotine, hydrocyanic acid and carbon monoxide from tobacco (22) and delta-9-tetrahydrocannabinol (THC) from marijuana (3) become concentrated in the remaining portion of the cigarette. Therefore, the alteration in smoking topography observed during the smoking of a single marijuana cigarette (7,21) could result from increased harshness of the smoke due to increased concentrations of irritating smoke components, including delta-9-THC (17), as rod filtration diminishes. Alternatively, saturation with the psychotropic effects of delta-9-THC might also explain the decrease in puff volume as a greater proportion of a marijuana cigarette is combusted. Previous studies have shown, however, that the level of intoxication from marijuana does not reach a peak until at least several minutes following completion of smoking (1, 9, 12), and that habitual marijuana smokers have poor ability to discriminate between cigarettes with different concentrations of delta-9-THC (2, 6, 10, 12), suggesting that nonpharmacologic factors are probably responsible for the change in smoking profile as cigarette length diminishes. The purpose of the present study was to compare the respiratory delivery of insoluble smoke particulates (tar), carbon monoxide and delta-9-THC from the distal versus the proximal

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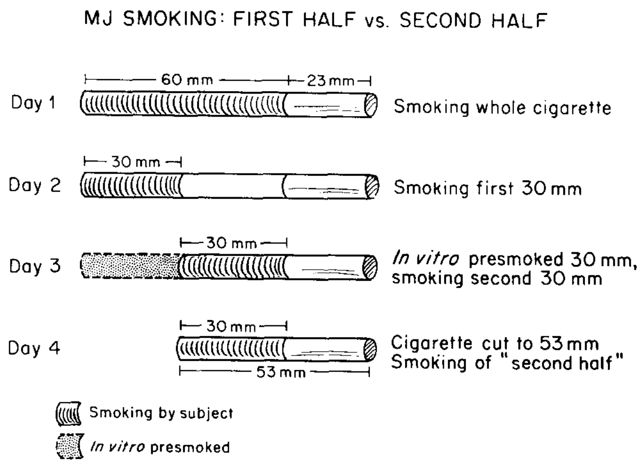


FIG. 1. Portion of marijuana cigarette smoked on each day of the study (see text).

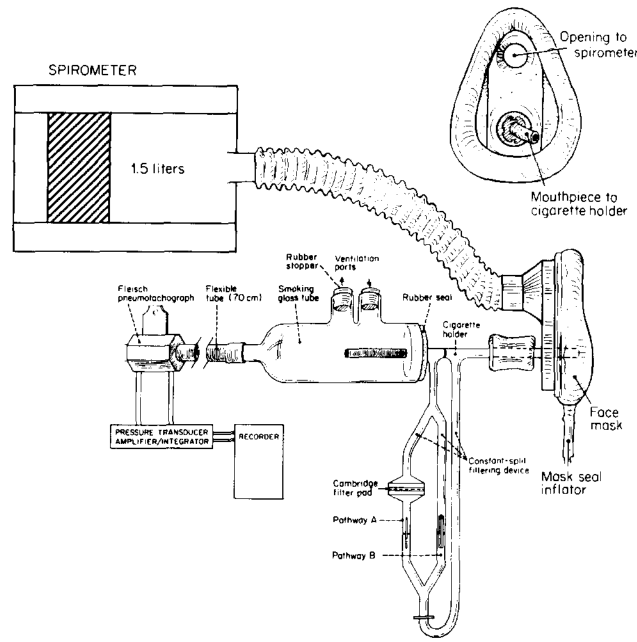


FIG. 2. Smoking apparatus used in marijuana smoking experiments. Proportional split filter device incorporated in smoking apparatus permits calculation of the amount of tar delivered to the smoker's mouth from the measured amount of tar trapped in the Cambridge filter pad (see text). Pathways A and B represent high resistance and low resistance pathways, respectively.

halves of a standard marijuana cigarette in man. Our hypothesis was that, compared to the distal half, the smoke generated by the proximal half of a marijuana cigarette delivers more tar, carbon monoxide and delta-9-THC to the respiratory tract of the smoker (despite possible changes in smoking profile that could limit delivery of these toxic substances), thus leading to potentially greater health effects and a higher level of intoxication.

## METHOD

Ten habitual smokers of marijuana (history of daily or near-daily use of marijuana for 5 or more years) who were without clinical evidence of cardiopulmonary disease were studied on 4 separate days. Subjects refrained from smoking marijuana for ≥12 hours and tobacco for ≥2 hours prior to each study visit. At each visit, subjects smoked nearly all or approximately one-half of a standard NIDA-supplied marijuana cigarette (~800–900 mg; 1.24% delta-9-THC; 83–85 mm), according to the scheme illustrated in Fig. 1. On day 1, subjects smoked the "entire" cigarette, consuming 60 mm of the cigarette rod and leaving a residual butt 23 mm in length. This butt length is similar to that which we previously observed in studies of the natural topography of smoking similar marijuana cigarettes supplied by NIDA (20). On day 2, subjects smoked only the first half (30 mm) of the cigarette. On day 3, the first 30 mm of the cigarette was presmoked with a syringe using a smoking profile characteristic of marijuana smoking (20), i.e., a 70-ml puff volume, 4-s puff duration and 30-s interpuff interval. Immediately thereafter, subjects smoked the second 30 mm of the cigarette, leaving a butt 23 mm long. On day 4, the first 30 mm of the cigarette was excised and subjects then smoked the second 30 mm, again leaving a butt length of 23 mm. While all subjects smoked an "entire" marijuana cigarette as described above on study day 1, the order of the remaining study days (days 2, 3 and 4) was randomized across the ten subjects.

The smoking apparatus used in these experiments has been described previously (20) and is shown in Fig. 2. The marijuana cigarette was inserted into a cigarette holder which perforated a rubber stopper sealing the proximal end of a 120-ml glass cylinder (smoking tube). The distal end of the smoking tube was connected to a 00 Fleish pneumotachograph for measurement of puff flow and volume. The smoking tube was vented through two ports between puffs to prevent accumulation of carbon monoxide and extinction of the cigarette. These ventilation ports were occluded during each puff so that the entire puff volume would be drawn through (and measured by) the pneumotachograph. The proximal end of the cigarette holder perforated another stopper which sealed the lower of two orifices in an airtight face mask. Subjects puffed on the mouthpiece extension of the cigarette holder that protruded into the face mask. After the full volume of each puff was taken, subjects opened their mouths and inhaled exactly 1.5 liters of room air from a rolling-seal spirometer connected to the upper orifice in the face mask.

During all four study sessions, puff volume and puff number were allowed to vary spontaneously, provided only that the specified length of cigarette was consumed. On the other hand, inhaled volume, breathholding time and interpuff interval were all held constant at 1.5 liters, 14 s and 30 s, respectively. That the full 1.5 liters were inhaled was verified by inductive plethysmography (18,19). After inhalation of the smoke-air mixture, subjects were instructed to hold their breath for 14 s, as timed by a stop-watch, before exhalation.

A previously described proportional filter device was incorporated into the cigarette holder to permit measurement of the amount of insoluble smoke particulates delivered to the smoker's mouth (14,20) (Fig. 2). This device diverted the mainstream smoke into two parallel pathways. Pathway A had a high resistance and pathway B a low resistance, such that approximately one-fifth of the smoke passed through the former and four-fifths through the latter. The high-resistance pathway contained a Cambridge filter pad which trapped virtually all of the smoke particulates, while the smoke traversing the low-resistance pathway was delivered to the smoker's mouth.

After each cigarette was smoked, the insoluble particulates (tar) trapped in the Cambridge filter pad were eluted with meth-

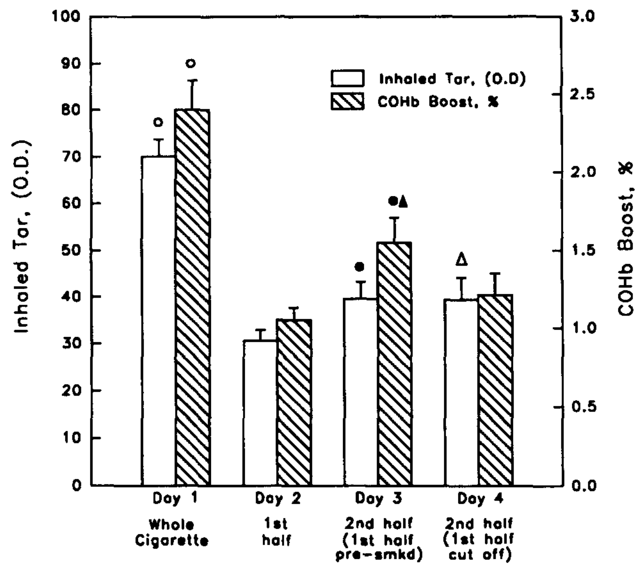


FIG. 3. Effect of portion of marijuana cigarette smoked on the amount of inhaled tar (in optical density units) (blank bars) and the pre- to postsmoking boost in blood carboxyhemoglobin concentration (in percent) (hatched bars). In this and subsequent figures, the error bars represent 1 standard error of the mean. ○ = significantly different from days 2, 3 and 4 ($p<0.001$). ● = significantly different from day 2 ($p<0.05$). △ = different from day 2 ($p<0.08$). ▲ = significantly different from day 4 ($p<0.01$).

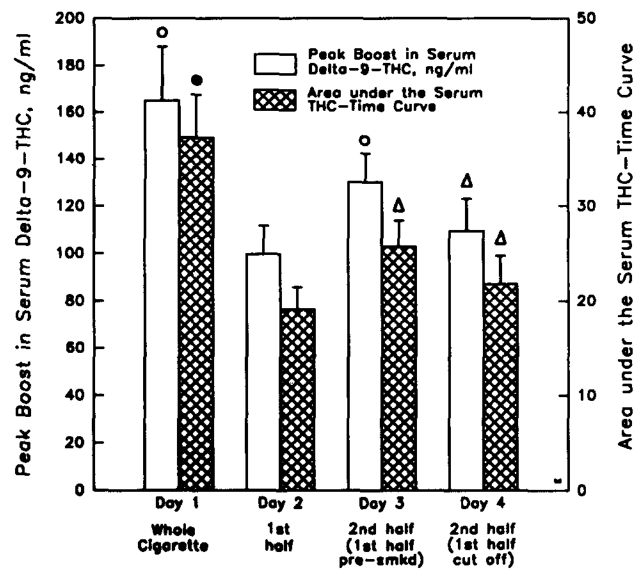


FIG. 4. Effect of portion of marijuana cigarette smoked on the pre- to postsmoking boost in serum delta-9-THC level (in ng/ml) determined 2 min after completion of smoking (open bars) and the area under the serum delta-9-THC concentration time curve determined using delta-9-THC levels measured before and 2, 15, 30 and 45 min after completion of smoking (cross-hatched bars). ○ = significantly different from days 2 and 4 ($p<0.02$). ● = significantly different from days 2, 3 and 4 ($p<0.03$). △ = significantly different from day 2 ($p<0.05$).

anol and analyzed using a spectrophotometer (wavelength 400 nm). Because a constant fraction of smoke particulates (approximately 17.2%) was retained in the filter, the actual quantity of tar delivered to the smoker could be calculated by multiplying the amount of particulates trapped in the Cambridge filter by 4.8.

An intravenous catheter was inserted at the beginning of each study session. Blood samples were withdrawn prior to smoking and at 2, 15, 30 and 45 min after completion of smoking for analysis of carboxyhemoglobin (COHb) using a CO-oximeter (Instrumentation Laboratory, model 282; Lexington, MA) and serum delta-9-THC by radioimmunoassay (16). Heart rate was measured before and 5 min after smoking. Twenty minutes after the completion of smoking, subjects rated their level of "high" on a scale of "0" to "10," "10" representing the greatest level of intoxication with marijuana ever experienced by each subject.

### *Data Analysis*

The quantity of inhaled tar and the pre- to postcigarette differences in blood carboxyhemoglobin, serum delta-9-THC concentration, heart rate and "high" were averaged for all 10 subjects for each of the four smoking conditions. Data were analyzed by one-way ANOVA (blocking by subjects) followed by Scheffe's multiple comparison test (4). $p$ Values $<0.05$ were considered statistically significant.

## RESULTS

The effect of the portion of the marijuana cigarette smoked on the amount of inhaled tar is shown in Fig. 3 (blank bars). Significantly more tar was inhaled from the second half of the cigarette (after the first half had been presmoked) than from the first half ($p<0.05$). Although more tar was also delivered from the second half (after the first half had been excised), this difference did not achieve statistical significance ($p<0.1$). As expected, the amount of tar inhaled from the entire cigarette was substantially greater than that from any half ($p<0.001$).

The effect of the portion of the marijuana cigarette smoked on the pre- to postsmoking boost in blood carboxyhemoglobin (COHb) detemined immediately prior to and 2 min following the completion of smoking is also shown in Fig. 3 (hatched bars). The COHb boost from the second half of the cigarette (after the first half had been presmoked) was significantly greater than that from either the first half or from the second half (after the first half had been excised) ($p<0.01$).

Figure 4 illustrates the effect of different portions of the marijuana cigarette on 1) the "peak" pre- to postsmoking boost in serum delta-9-THC concentration (difference between the THC concentrations measured before and 2 min after completion of smoking) and 2) the area under the serum delta-9-THC concentration-time curve calculated from the THC values measured at 2, 15, 30 and 45 min after smoking from which the presmoking baseline THC level was subtracted. Both the peak boost in THC levels and the area under the serum THC time curve were significantly greater following either second half (i.e., with the first half either presmoked or excised) than the first half of the cigarette ($p<0.05$). In addition, the peak boost in THC concentration was significantly greater following smoking the second half (after the first half had been presmoked) compared to the second half (after the first half had been excised). Not surprisingly, the peak boost in serum delta-9-THC and the area under the serum THC time curve were significantly higher after smoking the entire cigarette than any half.

Figure 5 shows the effect of the portion of the marijuana cigarette smoked on the peak change in heart rate (pre- to 5-min

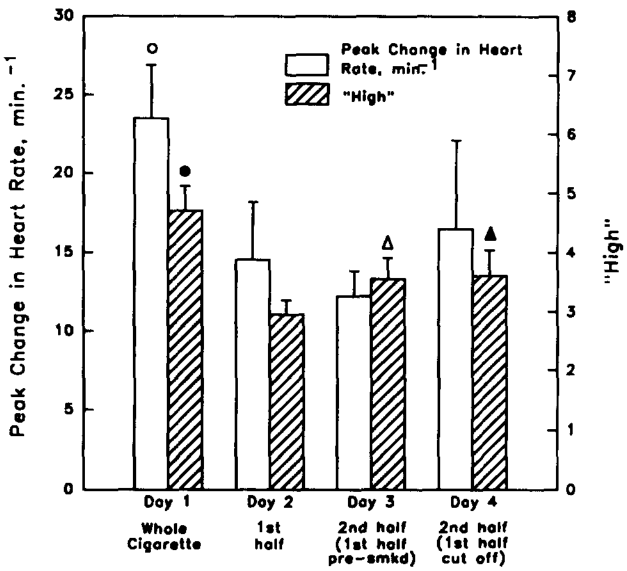


FIG. 5. Effect of portion of marijuana cigarette smoked on pre- to postsmoking increase in heart rate measured 5 min after completion of smoking (open bars) and level of intoxication ("high") assessed 20 min after completion of smoking (cross-hatched bars). ○ = significantly different from days 2 and 3 ($p \leq 0.01$). ● = significantly different from day 2 ($p<0.01$). △ = significantly different from day 2 ($p<0.03$). ▲ = different from day 2 ($p<0.07$).

postsmoking change) and the level of intoxication ("high") achieved 20 min after smoking. The "high," but not the boost in heart rate, was significantly greater following smoking the second half (with the first half presmoked) than the first half ($p<0.03$). The "high" after the second half (with the first half having been excised) also tended to be greater than that after the first half, but this difference failed to reach statistical significance ($p<0.07$).

No differences in smoking topography were noted across any of the four study sessions. On days 1, 2, 3 and 4, respectively, mean puff volume was $61.2 \pm 5.5$, $59.2 \pm 5.3$, $68.6 \pm 9.0$ and $63.4 \pm 5.9$ ml ($p>0.4$), while breathholding time averaged $15.2 \pm 0.4$, $15.7 \pm 0.8$, $15.0 \pm 0.5$ and $15.0 \pm 0.4$ s, respectively ($p>0.04$).

## DISCUSSION

The results of this study indicate that, compared to the distal half, smoking the proximal half of a standard marijuana cigarette (immediately after combustion of the first half) delivers more tar to the smoker's mouth (Fig. 3), leads to a greater boost in blood COHb (Fig. 3) and causes a greater rise in serum delta-9-THC (Fig. 4) and a greater level of intoxication ("high"), but no difference in heart rate (Fig. 5). Compared to the distal half of a full marijuana cigarette, smoking the proximal half (after excision of the uncombusted first half) also tended to deliver more tar ($p<0.08$) (Fig. 3), caused no difference in blood COHb boost (Fig. 3), produced a greater rise in serum delta-9-THC (but one that was significantly less than the rise caused by smoking the proximal half remaining after the distal half had been presmoked) (Fig. 4), and tended to cause a greater "high" ($p<0.07$), but no difference in pre- to postcigarette heart rate rise (Fig. 5).

The tendency for more tar to be delivered from the proximal compared to the distal half of a marijuana cigarette (irrespective of precombustion of the distal half) could simply be due to an effect of less rod filtration when the proximal half is smoked. On the other hand, a greater COHb boost from smoking the proximal compared to the distal half was noted when the distal half had been precombusted, but not when the distal half had been excised. Therefore, the observed difference in COHb boost cannot be attributed to a simple difference in rod filtration, but must be due to other factors. One possible explanation for the latter observation is that carbon monoxide (CO) generated from presmoking the distal half of the cigarette could be temporarily adsorbed in the proximal half and subsequently elaborated into the mainstream smoke during the smoking of the second half. A second possibility is that, while the second half of the cigarette was smoked, additional CO could be generated from carbonaceous material volatilized by prior combustion of the distal half and recondensed and concentrated in the cooler proximal half. Thirdly, more CO might be elaborated from the second half of the cigarette due to differences in burn rate resulting from an effect of precombustion of the distal half on the moisture content of the proximal half (13). Finally, loss of CO by diffusion through the cigarette paper decreases with each puff as the area of the paper decreases, causing an increase in CO per puff as butt length diminishes (22).

Our finding of a greater boost in serum delta-9-THC concentration following smoking the second half than the first half of a marijuana cigarette, after the first half had been either presmoked or excised, suggests that the reduced filtration through the smaller length of the cigarette rod when the second half was smoked contributed to a greater delivery of THC to the smoker. The additional observation that the boost in serum delta-9-THC was even greater when the second half was smoked after the first half had been presmoked, compared to simply excising the first half, suggests that another explanation in addition to simple differences in rod filtration is accounting for the greater THC boost from the second than the first half. It is possible, for example, that the THC that escapes destruction by the heat of pyrolysis in the first portion of the cigarette is concentrated in the cooler second portion, consistent with previous in vitro observations of Davis et al. (3). As the latter authors (3) have suggested, once this initial migration of THC into the cooler portion of the cigarette has occurred, further losses to pyrolysis are minimal, thereby allowing more THC to be translated into the mainstream smoke as the second half is smoked. These observations are also consistent with our finding of a significantly greater "high" after smoking the second half when the first half had been presmoked (but not after smoking the second half when the first half had been excised) compared to smoking the first half.

Our observations of a greater delivery of tar, carbon monoxide and delta-9-THC to the smoker from the second half of a marijuana cigarette, the first half of which had been presmoked, are in agreement with previous in vitro observations that smoke condensate, carbon monoxide and nicotine delivery increased as tobacco cigarette butt length decreased (22), and that the amount of delta-9-THC per unit weight of marijuana that was translated into mainstream smoke increased linearly as a function of the percent of the cigarette burned (3). In the present study, we failed to observe any effect of the portion of the marijuana cigarette smoked on smoking topography, in contrast to earlier findings both by ourselves (21) and others (9) of a reduction in puff volume during the smoking of the second compared to the first half of a marijuana cigarette. The reason for the discrepancy in these observations is not clear. Although it is possible that changes in smoking behavior down the burning length of a cigarette might moderate the increase in delivery of noxious smoke components from the proximal portion of the cigarette, the findings from the present study suggest that such changes in smoking profile may not occur. Moreover, if smoking alterations do occur during the smoking of a single cigarette, they still may not completely compensate for the greater yield of smoke constituents (per unit weight of cigarette) from the latter half of the cigarette.

An important clinical implication of the findings from this study is that smoking fewer marijuana cigarettes down to a shorter butt length to deliver more delta-9-THC and achieve a greater "high" will also result in the delivery of more tar and carbon monoxide to the smoker's respiratory tract than the consumption of a comparable amount of marijuana from more cigarettes smoked to a longer butt length. Because of the respiratory irritant and carcinogenic effects of some of the components of marijuana-derived tar (8,11), and the adverse effects of inhaled carbon monoxide on oxygen transfer in the lung, transport in the blood and delivery to the tissues (5,15), the common practice of smoking marijuana down to a short butt length may augment its potentially harmful effects on cardiorespiratory health.

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