*Victor C. Reeve,*[1] *B.A.; William B. Robertson,*[1] *B.S.;*
*Jim Grant,*[2] *M.D.; James R. Soares,*[2] *Ph.D.;*
*Emery G. Zimmermann,*[3] *M.D.; Hampshire K. Gillespie,*[4] *M.D.;*
*and Leo E. Hollister,*[4] *M.D.*

# Hemolyzed Blood and Serum Levels of $\Delta^9$-THC: Effects on the Performance of Roadside Sobriety Tests

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**ABSTRACT:** A pilot study was conducted to ascertain the range of induced hemolyzed blood/serum $\Delta^9$-tetrahydrocannabinol ($\Delta^9$-THC) concentrations in 58 human subjects. Subjects were tested within 5 min of smoking a $\Delta^9$-THC cigarette and then at half-hour intervals to 150 min. The subjects initially demonstrated a broad range of $\Delta^9$-THC hemolyzed blood levels, which settled within an hour to levels comparable to those measured in California drivers who had been stopped for impaired driving, arrested, and tested for $\Delta^9$-THC. Serum levels, when correlated with performance or roadside sobriety tests, demonstrated a broad range (5 to 183 ng/mL) of $\Delta^9$-THC levels and an "adaptation" effect in the subjects' perception of their own impairment.

Although this preliminary study was not a double-blind placebo experiment, the overall performance of human subjects demonstrated the "adaptation" effect, which may be a significant factor in making judgments while performing such complex tasks as driving. Also, the effects of the drug extended beyond the period of elevated $\Delta^9$-THC blood levels, perhaps because of THC metabolites that may contribute to impairment or the persistence of THC in the central nervous system. This pilot study will lay the groundwork for a program designed to determine the epidemiology and behavior correlates of marijuana use in motorists.

**KEYWORDS:** toxicology, tetrahydrocannabinol, driving

The correlation of blood alcohol concentration with impairment of physiological functions has been widely documented [*1,2*]. Some information is also available on the combination of $\Delta^9$-tetrahydrocannabinol ($\Delta^9$-THC) and alcohol and observable impairment [*3-6*]. However, little data are available correlating $\Delta^9$-THC blood levels with performance.

A recent survey of 1792 arrested impaired California motorists indicated a 14% incidence

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[1]Sacramento, CA.

[2]Receptor Research Institute, Glendale, CA.

[3]Director, Sleep Disorders Clinic, Departments of Anatomy and Neurology, School of Medicine, University of California Los Angeles, CA (and Receptor Research Institute, Glendale, CA).

[4]Veterans Administration Hospital, Palo Alto, CA.

of $\Delta^9$-THC in their submitted blood samples [7]. Every one of the arrested impaired drivers with $\Delta^9$-THC in their blood (1250) failed the Standard California Highway Patrol (CHP) Roadside Sobriety Tests (RSTs) [8]. The RSTs are described in the Highway Patrol Guide 70.4, "Drinking Driver Enforcement Guide" [8], and are generally used by law enforcement officers to document suspected impairment. The subjects' test performances, their general reaction at the roadside stop, and the observed prestop vehicular movements are instrumental in the traffic officer's final decision to arrest, detain, or release the stopped motorist.

A pilot study was designed to ascertain the range of hemolyzed blood and serum $\Delta^9$-THC levels that are associated with observable impairment in RSTs. Another purpose of the study was to ascertain the feasibility and design of an extensive double-blind placebo study involving marihuana and alcohol in which test subjects will drive instrumented cars on a closed course [9].

## Experimental Design

### *Subjects*

The volunteer subjects consisted of females and males ranging from 21 to 52 years old. The 58 marihuana smokers' habits were grouped in three categories: 18 light smokers (one or two times a month or less), 25 medium (one or two times a week), and 15 heavy (one or two times a day).

### *Administration of Drug and Testing*

Each volunteer was instructed to smoke 2-g National Institute on Drug Abuse (NIDA) $\Delta^9$-THC cigarettes containing 18 mg of $\Delta^9$-THC until he/she achieved a social high. The subjects consumed, within 10 min each, from one to four of the NIDA cigarettes. Just before smoking and at 5, 30, 90, and 150 min afterwards, blood samples (approximately 15 mL) were drawn. The subjects were then escorted to a separate test facility and interviewed by an experienced uniformed CHP officer.

### *RST Description and Scoring*

RSTs were described, demonstrated, and administered. The subject was then asked to rate his/her own impairment on a scale of 0 to 9, with 0 indicating no detectable effect and 9 being the greatest high the subject has experienced, or what he/she would define as "completely stoned." The officer was also interviewed as to his assessment of the subject's impairment on a similar rating scale. The subject's performance was documented by a videotape recording.

Driving performance and RSTs are the criteria used by CHP officers to evaluate whether a driver may be on drugs. A scoring system that considered the subject's rating in the RST was established accordingly:

- 0—The officer would not detain.
- 1-2—The officer would remove the subject from the highway but would not make an arrest.
- Greater than 2—The officer would arrest the subject and would demand blood, breath, or urine samples to establish corroborative physical evidence of impaired driving.

Self-rating studies [10-13] have concluded that a rating greater than 3 on a 10-point scale usually indicates considerable impairment or drug effect. The rating system established with the officers was that a score greater than 2 was considered sufficient for arrest and detention. This rating was classified as "objective." The assessment of "impaired" was arrived at by the CHP officers conducting the test and by a second observer who independently rated the level

of impairment. Later playback of videotape recordings of the performances before analytical blood levels were cross-indexed was also used in final assessment of the subject's condition.

Each RST was scored from 1 to 4, where 1 was satisfactory, 2 and 3 indicated increasing decrements in performance, and 4 indicated failure. Two or more performance decrements in the performance of the RSTs automatically resulted in a 4.

*Blood*

Blood specimens were collected in Vacutainer® gray-top (10-mg disodium ethylenediaminetetraacetic acid [EDTA] and 20-mg sodium fluoride) tubes and Corvac® (silicon grease-coated interior) serum blood collection tubes. The preservative and anticoagulant chemicals contained in the gray-top blood collection tubes, when well mixed, caused hemolysis of the blood in a relatively short period. The Vacutainer tubes were refrigerated until shipped. The centrifuged serum samples were withdrawn from the Corvac tubes within 30 min of collection and aliquots were frozen in plastic (polyethylene) tubes until they could be shipped frozen for radioimmunoassay.

*Method of Analysis*

Hemolyzed blood and serum specimens were analyzed for $\Delta^9$-THC by a previously described $^3$H-radioimmunoassay procedure [*14, 15*]. Hemolyzed blood samples (Table 1) were analyzed for $\Delta^9$-THC by a previously described high-pressure liquid chromatography/mass spectrometry technique [*16*].

*Data Analysis*

All data relating to the documentation of the RSTs were tabulated before any correlation with blood and serum assay results. Subjects given an overall rating greater than 2 were considered to have failed in the objective rating, and subjects rating themselves (subjective rating)

TABLE 1—*Comparative assays of hemolyzed blood from smokers (actual* $\Delta^9$-THC levels unknown).[a]

| RIA | GC/MS-Electron Impact |
|---|---|
| 0 | 7.6 |
| 29 | ...[b] |
| 18 | 14.9 |
| 8 | 5.5 |
| 6 | 6.6 |
| 17 | 5.9 |
| 16 | 31.7 |
| 0 | 3.0 |
| 0 | 5.4 |
| 0 | 1.8 |
| 0 | 0 |
| 33 | 125.3 |
| 14 | 23.6 |
| 7 | 6.3 |
| 0 | 7.8 |
| BLANKS | |
| 0 | 6.0 |
| 0 | 1.4 |
| 0 | 2.0 |

[a]For discussions of analytical methods, see Ref *14* for radioimmunoassay (RIA) and Ref *15* for gas chromatography/mass spectrometry (GC/MS).

[b]Not assayed.

were considered to have failed if they scored themselves greater than 3. These ratings were then compared with blood and serum $\Delta^9$-THC levels.

## Results

### *Quality Control*

A total of 69 blind controls were included with the 610 blood and serum samples. These included 16 negative samples (blanks), 42 repeat submissions (repeats), and 11 known positives. In addition, 15 sample aliquots of hemolyzed blood from similar smoking subjects were submitted with 3 blank hemolyzed blood samples to 2 independent laboratories for comparative analyses by radioimmunoassay [*14*] and gas chromatography/mass spectrometry [*16*]. The final quality control results and the comparative assays are outlined in Tables 1 and 2.

### *Experimental Subjects*

Serum and blood concentrations of $\Delta^9$-THC developed during the RST are outlined in Tables 3 through 7, according to smoking habit. Figure 1 illustrates the mean and range of $\Delta^9$-THC blood and serum levels of the overall subject population. Whole blood $\Delta^9$-THC levels are generally lower than serum levels from the same person, presumably because of

TABLE 2—*Blind quality control samples,*[a] *ng/mL.*

| Parameter | Blood | Serum |
|---|---|---|
| Blanks | | |
| Mean | 0-5.5 | 0-5.5 |
| Standard deviation | 0 | 0 |
| Range | 0 | 0 |
| Number | 11 | 5 |
| Repeats | | |
| Mean | 2.5 | 17.4 |
| Standard deviation | 1.8 | 8.21 |
| Range | 0-24 | 0-40 |
| Number | 22 | 20 |
| Spikes | | |
| Mean | 17.5 | 380 |
| Standard deviation | 2.0 | 14.14 |
| Range | 15-20 | 0-40 |
| Number | 2 | 9 |

[a]Samples assayed at 5.5 ng/mL or less were reported as 0.

TABLE 3—*Serum concentrations of THC in 15 heavy users of* Cannabis.[a]

| Time, min | Mean | Standard Deviation | Range |
|---|---|---|---|
| 0 | 6.5 | 6.5 | 0-20 |
| 5 | 84.1 | 41.1 | 24-183 |
| 30 | 29.8 | 7.7 | 20-45 |
| 90 | 14.6 | 5.8 | 0-25 |
| 150 | 8.9 | 5.8 | 0-18 |

[a]Nine subjects had detectable THC. All values in ng/mL (assay sensitive to 5.5 ng/mL). Thirteen subjects smoked more than one cigarette.

TABLE 4—*Serum concentrations of THC in 25 medium users of* Cannabis.[a]

| Time, min | Mean | Standard Deviation | Range |
|---|---|---|---|
| 0 | 8.3 | 2.3 | 6-12 |
| 5 | 61.2 | 29.9 | 16-108 |
| 30 | 18.6 | 8.0 | 0-32 |
| 90 | 9.7 | 5.9 | 0-20 |
| 150 | 5.3 | 5.1 | 0-13 |

[a]Six subjects had detectable THC. All values in ng/mL (assay sensitive to 5.5 ng/mL). Nine subjects smoked more than one cigarette.

TABLE 5—*Serum concentrations of THC in 18 light users of* Cannabis.[a]

| Time, min | Mean | Standard Deviation | Range |
|---|---|---|---|
| 0 | 0.6 | *[b] | *[b] |
| 5 | 46.7 | 32.6 | 18-132 |
| 30 | 11.3 | 6.7 | 0-23 |
| 90 | 5.3 | 4.8 | 0-14 |
| 150 | 1.7 | 3.2 | 0-9 |

[a]Two subjects had detectable THC below 5.5 ng/mL. All values in ng/mL (sensitivity of assay 5.5 ng/mL). All subjects smoked only one cigarette.

[b]Values not included because detectable THC levels in 0- to 5-ng/mL range are below assay sensitivity.

TABLE 6—*Serum concentrations of THC in 22 subjects smoking more than one cigarette (range 1¼ to 4).*[a]

| Time, min | Mean | Standard Deviation | Range |
|---|---|---|---|
| 0 | 3.8 | 4.8 | 0-13 |
| 5 | 79.1 | 37.8 | 26-134 |
| 30 | 28.4 | 8.2 | 12-45 |
| 90 | 13.9 | 4.4 | 0-25 |
| 150 | 8.7 | 5.4 | 0-18 |

[a]Nine subjects had detectable THC. All values in ng/mL (sensitivity of assay 5.5 ng/mL).

TABLE 7—*Serum concentrations of THC in 36 subjects smoking one cigarette.*[a]

| Time, min | Mean | Standard Deviation | Range |
|---|---|---|---|
| 0 | 2.4 | 5.5 | 0-22 |
| 5 | 53.9 | 32.1 | 16-132 |
| 30 | 14.7 | 7.9 | 0-32 |
| 90 | 7.1 | 5.2 | 0-17 |
| 150 | 3.3 | 4.5 | 0-13 |

[a]Eight subjects had detectable THC. All values in ng/mL (sensitivity of assay 5.5 ng/mL).

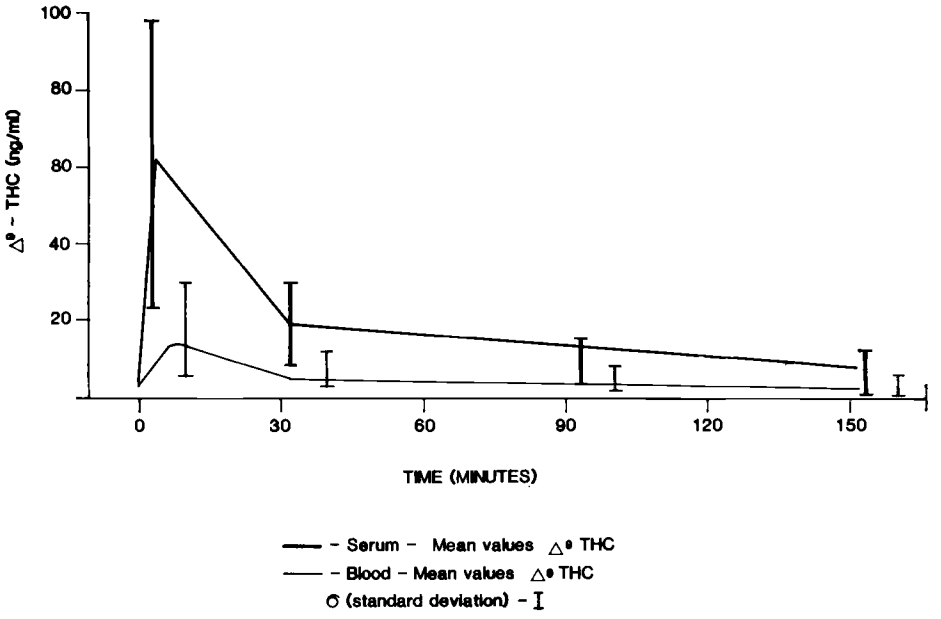


FIG. 1—*Mean $\Delta^9$-THC levels versus time for 58 subjects (assay sensitivity 5.5 ng/mL).*

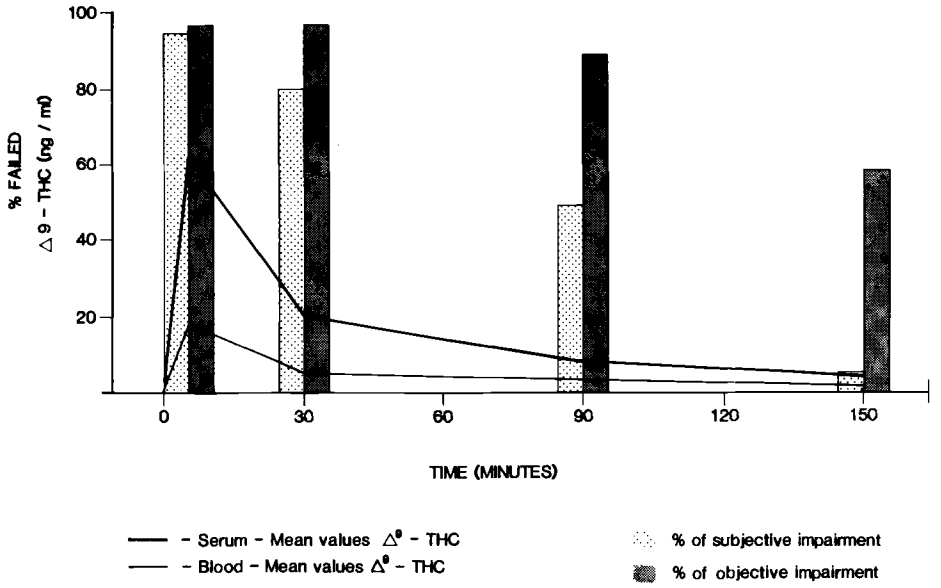


FIG. 2—*General impairment as related to $\Delta^9$-THC levels over time for 58 subjects (assay sensitivity 5.5 ng/mL).*

dilutions by red cells. Ordinarily one would expect that blood levels should be about 55% of serum levels, but $\Delta^9$-THC is not stable in blood and tends to decrease in concentration under a variety of storage conditions [*17*].

Figure 2 displays the correlation of both $\Delta^9$-THC levels and percentage of subjects rated failed by observers with subjective evaluations of degree of "high." Objective (98.4%) and subjective (95%) impairment were maximal at 5 min, but decreased at different rates as time

after smoking increased. Although 95% of the smokers considered themselves to be functioning normally at the time, 57.6% remained objectively impaired at 2½ h.

The RST components (finger-to-nose, Rhomberg, standing on one foot, and heel-to-toe) were compared with $\Delta^9$-THC serum levels. The failure rate was greatest (84 to 95%) at 5 min and diminished with time. These results correlated more closely with $\Delta^9$-THC serum concentrations than did overall (objective) impairment.

Objective RST parameters were correlated with $\Delta^9$-THC level at all times after intoxication. All subjects failed the RST at high (>40 ng/mL) or medium (21 to 39 ng/mL) $\Delta^9$-THC concentrations, while a majority (80%) failed at low (3 to 20 ng/mL) levels. Over 86% of the volunteers rated themselves impaired at medium or high $\Delta^9$-THC concentrations, but only 38% considered themselves impaired at low levels.

The $\Delta^9$-THC levels of people who passed RSTs and their smoking habits are outlined in Table 8. There is a greater spread in the serum $\Delta^9$-THC levels of the passing heavy users, indicating a greater tolerance in this population (5 to 22 ng/mL). The variation in level (5 to 10 ng/mL) is less in the "medium" and even less in the "light" group (5 to 8 ng/mL).

One subject did not inhale the smoke from the $\Delta^9$-THC cigarette and was rated consistently as unimpaired throughout the RST. His blood and serum levels confirmed zero $\Delta^9$-THC. This factor was unknown to the testing officers, to control against undue bias, since the officers were aware that marihuana cigarettes were being smoked by the subjects.

A particularly striking example was leg tremor observed in the standing-on-one-leg test, which as present in 86% of those with high $\Delta^9$-THC body fluid concentrations but in only 39% with low concentrations. The leg tremor was described as a hard-to-control shivering of the weight-bearing knee joint. Interviewed subjects attributed the effect to a feeling of weakness in the joints (arms and legs) that resulted from smoking the marihuana cigarettes.

Individuals who were heavy users smoked more $\Delta^9$-THC cigarettes (mean 1.6) and achieved higher $\Delta^9$-THC serum levels (mean 84.1 ng/mL) than did medium (1.3 cigarettes, 61.2 ng/mL) or light (1.0 cigarettes, 46.7 ng/mL) users. However, just as many heavy smokers were judged impaired as medium (100%) or light (92 to 94%) users with equivalent $\Delta^9$-THC serum concentrations.

## Conclusions

The data summarized in Fig. 2 demonstrate that general impairment as judged by experienced CHP officers and trained observers does not correlate with $\Delta^9$-THC blood levels.

Tables 3 through 7 and Fig. 1 demonstrate a considerable range of $\Delta^9$-THC concentra-

TABLE 8—*Serum concentrations of THC in subjects who passed RSTs, correlated by smoking habit.*

| $\Delta^9$-THC Serum Level, ng/mL | Number of Pass Points[a] by Smoking Habit | | |
|---|---|---|---|
| | Heavy | Medium | Low |
| 0-5 | 5 | 22 | 29 |
| 6-10 | 9 | 10 | 1 |
| 11-15 | 5 | ... | ... |
| 16-20 | 1 | ... | ... |
| 22 | 1 | ... | ... |
| Mean | 9.57 | 5.94 | 5.07 |
| Standard deviation | 4.60 | 1.56 | 0.54 |
| Range | 0-22 | 0-10 | 0-8 |
| Total potential pass points | 75 | 125 | 90 |
| Percent of passes | 20% | 25.6% | 33.3% |

[a]Pass points are successful observer ratings of completion of RSTs from time 0 to 150 min after smoking.

tions. Despite the serum and blood concentration range (0 to 18 ng/mL), the majority of subjects were rated impaired by observers. The data in Table 8 demonstrate a tolerance effect in the $\Delta^9$-THC serum levels of subjects who passed impairment tests at various times.

This study indicates that, as with alcohol [*18*], subjective judgments of impairment after inhalation of $\Delta^9$-THC exhibit an adaptational effect. That is, a given level of $\Delta^9$-THC produces less of a sense of intoxication "on the way down" than "on the way up."

There is a persistent effect of $\Delta^9$-THC that does not correlate directly with serum and blood levels; substances other than $\Delta^9$-THC may be associated with impairment. The subjects initially reported a degree of intoxication that correlated with serum and blood $\Delta^9$-THC level. However, with time, the subjective evaluation demonstrated a divergence from observer rating of performance. This indicates that the subjects did not appreciate their degree of impairment, as demonstrated by the disparity between their objectively rated performance and their subjective evaluations.

Correlations of RSTs with $\Delta^9$-THC levels compared to independent ratings of driver's license examiners and CHP officers to be performed on a double blind/placebo basis (in progress) are needed to document the ability of the trained law enforcement officer to detect marijuana-impaired drivers. Impaired subjects do not rate themselves as "under the influence" when they are judged to be so by observers.

Questions that need to be addressed in future studies are:

- What are the separate effects of alcohol and marihuana on driving skills and, by extension, on traffic safety?
- What association exists between impaired driving as detected by law enforcement officials and the presence of these substances as detected by laboratory procedures?
- What are the quantitative aspects of the relationship among types of substance, either alone or in combination; dosage and time since ingestion; level in various biological compartments such as breath, blood, and urine; and driving performance?
- Based on the preceding, what legislation is needed to minimize the social cost of the abuse of marihuana, alcohol, and marihuana combined with alcohol on the highways?

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Address requests for reprints or additional information to
V. C. Reeve
4171 Stillmeadow Way
Sacramento, CA 95821