The Use of Triazolam in Older Patients With Periodic Leg Movements, Fragmented Sleep, and Daytime Sleepiness

Michael H. Bonnet and Donna L. Arand

1Long Beach VA Hospital, and the University of California, Irvine.
2The University of California, Los Angeles.

Many studies have shown a relationship between fragmented nocturnal sleep and daytime sleepiness. In the current study, 11 patients, aged 55-75, were identified with fragmented nocturnal sleep secondary to periodic leg movements and objective daytime sleepiness as verified by the Multiple Sleep Latency Test (MSLT). In a double-blind, repeated measures, cross-over design, patients had three nights of treatment with placebo, 0.125 mg of triazolam, or 0.25 mg of triazolam following an adaptation night. Although total leg movements were not changed, the medication increased total sleep time and sleep efficiency while decreasing the number of stage changes. Generally, daytime performance and objective alertness were significantly improved following the use of triazolam. It was concluded that acute use of triazolam, particularly the 0.125 mg dose, could improve sleep and daytime function in older patients with periodic leg movements, fragmented sleep, and daytime sleepiness.

Decreased daytime alertness is a frequent complaint in persons over 55 years of age. Recent work has shown that many older individuals may have decreased function as a result of fragmented nocturnal sleep. Carskadon et al. (1,2) found that 33% of healthy older individuals without sleep complaint had over 100 disruptive events (myoclonic jerks and/or primarily central apnea) during sleep and subsequent daytime nap latencies of less than 9 minutes. The remaining older subjects studied had normal nap latencies (in excess of 15 min) and fewer than 35 disruptive events during their sleep. A significant negative correlation was found overall between nap latencies and the number of transient arousals on the prior night.

Other work (3) has shown that normal young adults whose sleep was briefly disrupted as few as 40 times per night (i.e., once after each 10 min of sleep) showed degraded daytime performance and increased daytime sleepiness. This study also showed that if normal sleep was allowed for 2.5 hours and then followed by frequent sleep disruption, performance on the following day was significantly better than when periodic arousals were made every 10 minutes throughout sleep, even though total sleep time was greater in the latter condition.

These studies indicate that sleep fragmentation is related to daytime sleepiness. However, as little as 2-3 hours of consolidated sleep appear to minimize daytime sleepiness. This suggests that a relatively short period of consolidated sleep may also be restorative in patients diagnosed as having periodic leg movements (PLMS) with fragmented sleep and a complaint of excessive sleepiness (4). These patients have traditionally not been considered as candidates for benzodiazepine therapy because the long metabolic life of benzodiazepines could cause additional residual daytime sleepiness. As a result, most treatment studies of PLMS have studied insomniacs (5-9) and/or avoided objective verification of sleepiness (10-12). We hypothesized that the use of the short-acting benzodiazepine triazolam at doses which have been shown to not result in daytime hangover sedation would decrease arousals, consolidate sleep, and improve objective alertness the following day.

Method

Subjects. — Subjects were required to be between 55 and 75 years of age, in good health, and to have a complaint of daytime sleepiness. Patients had typically been referred to the Sleep Disorders Center with a report of increased need for sleep and, usually, a report of restless sleep or leg jerks during sleep. The patients were given a physical exam and it was determined that they did not suffer from chronic pain or any uncontrolled neurologic, hematologic, hepatic, renal or cardiovascular disease. At the time of study, patients were not using any prescription tranquilizers or hypnotics. Potential subjects with significant psychopathology (MMPI clinical scales in excess of 2 SD from the mean), uncontrolled diabetes (urine screen), thyroid dysfunction (T4 screen), or historical evidence of narcolepsy or obstructive sleep apnea (obtained via a standard sleep history) were excluded.

Screening. — Consenting subjects were scheduled for a sleep laboratory screening night followed by daytime testing and Multiple Sleep Latency Test (MSLT). Entry into the study proper required the presence of periodic leg movements as traditionally defined (13). It was additionally required that the periodic leg movements result in at least 80 brief EEG arousals or awakenings and that median latencies were less than 10 minutes. The arousal criterion was based on our work with periodic arousal from sleep (3) as well as the Carskadon et al. (1,2) data. The 10-minute MSLT value was used based on the (1,2) data and the common sleep

M139
center rule that nap latencies of less than 10 minutes indicate at least borderline pathological sleepiness. Patients with more than five mixed or obstructive apneas per hour of sleep, five or more central apneas per hour, or a combination of six or more central and obstructive apneas per hour of sleep were excluded from the study.

Procedure. — After screening, each subject participated for a total of 12 nights. The nights were divided into three 4-night conditions: (a) placebo; (b) 0.125 mg triazolam; and (c) 0.25 mg triazolam. Each 4-night condition was run on four consecutive week nights. On the first night of each 4-night condition, subjects always received a placebo. During the placebo condition, $S$s received placebo on all four nights. In each medication condition, subjects received the same dose of active medication on the final three nights. Each 4-night condition was separated from the next by 10 nights so that subjects spent the same nights of the week in the laboratory on consecutive weeks. On each night, a pill was taken 30 minutes prior to normal bedtime, which was held constant throughout the study and occurred between 2200 and 2400. Awakening time was also held constant for each subject throughout the study. The pills were matched and conditions were assigned randomly in a double-blind fashion. Of the four nights in each condition, three (the first, second, and fourth) were spent in the sleep laboratory, and the third night was spent at home with medication or placebo. Following all nights spent in the laboratory, subjects remained throughout the day for MSLT (0800, 1000, 1200, 1400, 1600, 30-min addition tests (0700, 1100, 1430), 30-min auditory vigilance tests (0730, 1130, 1500), Profile of Mood States (0840, 1040, 1240, 1540), and short-term memory tests (1030, 1550). The addition tests were scored for number of correctly completed and incorrectly completed problems; the auditory vigilance was scored for hit rate and false alarm rate, and the short-term memory test was scored for number of words correctly recalled.

Subjects were instructed to take no psychotropic or sedative medication for seven days prior to the beginning of the study and throughout the course of the study. Subjects also refrained from alcohol ingestion for two days prior to the study and during the laboratory sessions. Subjects were asked to refrain from caffeine consumption during the study, and no caffeine containing coffee and beverages were recommended.

Patients arrived at the laboratory each evening approximately one hour prior to their normal bedtime and were prepared for standard polysomnographic recordings (14) including EEG, EOG, EMG, EKG, airflow, as measured by SomniProbe™ nasal and oral thermistor, chest and abdominal movements (cardiopneumograph), left and right anterior tibialis EMG, and %SaO2 (Biocor model II or Ohmeda model 3700). Sleep records were scored for all standard polysomnographic variables (15). Apreas, leg movements from either leg, and all brief EEG arousals were scored in each record. Leg movement scoring criteria included an initial increase in leg EMG to at least double the background EMG lasting 0.5 to 5.0 sec. All leg movements were scored with the requirement that leg EMG increases occurred before any other sign of arousal but without regard to bursts, because occasional isolated leg jerks associated with awakening or arousal exist in all patients with PLMS and are missed by traditional scoring. An EEG arousal was defined as a 3-second change in ongoing EEG including a burst of alpha. EEG speeding or chin EMG increase. Reliability of leg movement scoring and EEG arousal scoring was assessed along with reliability of sleep stage scoring. It was found that the scoring of leg movements and arousals was more difficult than scoring of normal sleep stages. As a result, an 85% level of agreement was accepted. On occasions when reliability was below this level, disagreements were checked and rectified, and the record was rescoring by the primary scorer.

Data from the study proper were analyzed by repeated measures analysis of variance (ANOVA). Nocturnal sleep, leg movement, and respiratory variables were analyzed by comparing the final two laboratory nights on the placebo week with both laboratory nights of administration of triazolam 0.125 mg and both laboratory nights of administration of triazolam 0.25 mg. The analyses had terms for medication condition (2 df), night of administration (1 df), and night × condition interaction (2 df). No significant night × condition interactions were found, and the interaction variance was therefore pooled with error to test the main effects for night and condition. Where significant F-values were found at p < .05 with Greenhouse-Geisser criterion, pairwise comparisons were performed with the Neuman-Keuls procedure at the .05 level and based upon Greenhouse-Geisser df. Significant differences are noted in the tables.

RESULTS
A total of 11 (7 male and 4 female) subjects were qualified and enrolled in the study. Subjects had a mean age of 65 (range 57–74) and an average weight of 157 lbs. (range 110–225).

Sleep data. — A summary of sleep stage values in the three conditions is presented in Table 1. While time in bed remained constant, there was a significant increase in total sleep time of about 25 minutes in both medication conditions as compared to placebo. This increase was also reflected in significantly increased sleep efficiency and significantly decreased % Wake. This increase in sleep was primarily in % Stage 2, which was also increased in both medication conditions as compared to placebo.

In terms of awakening/disturbance variables, triazolam significantly reduced the number of sleep stage changes at the 0.25 mg dose level as compared to placebo (115 vs 135 stage changes), but the medication had no significant effect on total awakenings or early final awakening, which were low in all conditions.

Respiratory data. — As expected from screening, these subjects did not have significant respiratory disturbance on placebo nights. Triazolam had no clinically or statistically significant impact on any of the seven respiratory variables measured.

Leg movement and arousal data. — Leg movement and arousal data are summarized in Table 1. These data were analyzed by the entire night and by thirds of the night in an attempt to find medication time course effects. However, sig-
Table 1. Sleep Variables

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>0.125mg</th>
<th>0.25mg</th>
<th>( F ) (df) Condition</th>
<th>( G - G ) ( P^* )</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time in bed (min)</td>
<td>490</td>
<td>487</td>
<td>492</td>
<td>0.85 (37)</td>
<td>.05</td>
<td>PL &lt; all 7</td>
</tr>
<tr>
<td>Total sleep (min)</td>
<td>403</td>
<td>423</td>
<td>427</td>
<td>4.02 (21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep latency (min)</td>
<td>.15</td>
<td>.10</td>
<td>9</td>
<td>1.27 (33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stage 1</td>
<td>16</td>
<td>15</td>
<td>13</td>
<td>1.28 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stage 2</td>
<td>47</td>
<td>52</td>
<td>55</td>
<td>6.35 (40)</td>
<td>.01</td>
<td>PL &lt; all 7</td>
</tr>
<tr>
<td>% Stage 3</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>3.14 (30)</td>
<td>.1</td>
<td></td>
</tr>
<tr>
<td>% Stage 4</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0.79 (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stage REM</td>
<td>17</td>
<td>18</td>
<td>17</td>
<td>1.09 (34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Stage W</td>
<td>17</td>
<td>13</td>
<td>13</td>
<td>3.66 (29)</td>
<td>.05</td>
<td>PL &gt; .125</td>
</tr>
<tr>
<td>Sleep efficiency</td>
<td>83</td>
<td>87</td>
<td>87</td>
<td>3.89 (29)</td>
<td>.05</td>
<td>PL &lt; all 7</td>
</tr>
<tr>
<td>Number of awakenings</td>
<td>28</td>
<td>25</td>
<td>26</td>
<td>1.27 (37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early final awakening (min)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>1.52 (21)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage changes</td>
<td>135</td>
<td>122</td>
<td>115</td>
<td>3.70 (40)</td>
<td>.05</td>
<td>PL &gt; .25</td>
</tr>
<tr>
<td>Leg movements</td>
<td>257</td>
<td>293</td>
<td>304</td>
<td>1.96 (46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEG arousals</td>
<td>203</td>
<td>214</td>
<td>205</td>
<td>0.28 (70)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( ^* G - G \) \( P \) = Greenhouse-Geisser Probability Level.

\( ^7 \) PL = Placebo.

Table 2. Subjective Sleep Values

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>0.125mg</th>
<th>0.25mg</th>
<th>( F ) Condition</th>
<th>( G - G ) ( P^* )</th>
<th>Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency (min)</td>
<td>40</td>
<td>28</td>
<td>20</td>
<td>6.20</td>
<td>.01</td>
<td>.125 = .25 &lt; PL</td>
</tr>
<tr>
<td>Latency compared to usual latency( ^* )</td>
<td>4.4</td>
<td>4.0</td>
<td>3.1</td>
<td>9.89</td>
<td>.01</td>
<td>.25 &lt; .125 = PL</td>
</tr>
<tr>
<td>Wakefulness</td>
<td>3.9</td>
<td>2.4</td>
<td>1.7</td>
<td>6.25</td>
<td>.02</td>
<td>.125 = .25 &lt; PL</td>
</tr>
<tr>
<td>Wake time (min)</td>
<td>41</td>
<td>30</td>
<td>19</td>
<td>3.06</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td>Total sleep (hr)</td>
<td>6.5</td>
<td>7.4</td>
<td>7.4</td>
<td>2.14</td>
<td>.11</td>
<td></td>
</tr>
<tr>
<td>Total sleep compared to usual sleep( ^* )</td>
<td>1.7</td>
<td>1.7</td>
<td>1.1</td>
<td>8.00</td>
<td>.01</td>
<td>.25 &lt; .125 = PL</td>
</tr>
<tr>
<td>Sleep depth</td>
<td>2.0</td>
<td>1.5</td>
<td>1.4</td>
<td>8.80</td>
<td>.01</td>
<td>.125 = .25 &lt; PL</td>
</tr>
<tr>
<td>Sleep quality( ^* )</td>
<td>3.0</td>
<td>2.1</td>
<td>1.9</td>
<td>8.36</td>
<td>.01</td>
<td>.125 = .25 &lt; PL</td>
</tr>
<tr>
<td>ADL alertness( ^* )</td>
<td>4.3</td>
<td>4.2</td>
<td>4.0</td>
<td>0.60</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Medication effectiveness( ^* )</td>
<td>1.7</td>
<td>2.2</td>
<td>2.8</td>
<td>7.16</td>
<td>.02</td>
<td>PL &lt; .25</td>
</tr>
</tbody>
</table>

\( ^* G - G \) \( P \) = Greenhouse-Geisser Probability Level.

\( ^* \) On these scales, lower numbers correspond to increased sleep quality, depth, etc.

\( ^* \) On this scale, higher numbers correspond to increased efficacy.

Significant time course effects or overall effects were not found for leg movements or EEG arousals. Several additional analyses attempting to control total leg jerks, total sleep time, and time intervals between leg jerks were performed. None of the analyses consistently suggested significance.

Subjective ratings of sleep. — Subjective sleep report data can be found in Table 2. In terms of subjective report, the medication significantly reduced sleep latency, reduced awakenings, increased depth of sleep, and improved sleep quality. The medication was also considered significantly effective by subjects.

Daytime performance. — The analysis of the performance data differed from the analysis of the sleep in two respects. First, a significant learning effect exists for the performance tasks used in the study. Learning and laboratory adaptation effects were examined by analyzing the correct addition data, vigilance hit rate data and MSST and data for systematic changes across the five placebo nights in the study. Correct additions increased significantly across placebo nights (\( F(4,58) = 20.76, p < .01 \); correct problems increasing from 87 to 103). Vigilance hit rate increased nonsignificantly across placebo nights (\( F(4,58) = 0.93 \); hit rate increasing from .52 to .59). Nap latencies increased significantly across placebo nights (\( F(4,125) = 4.79, p < .01 \); latencies increasing from 5.8 to 9.1 minutes). To control for learning effects, a placebo day averaging method suggested by Lubin et al. (16) and currently used elsewhere (3,17,18) was performed. A linear regression line was standardly fit through all five placebo days in the study. This regression equation was then used to predict performance on postmedication days based on the placebo day values. The placebo-predicted performance values were then compared to the actual observed performance values. This meant that there was a corresponding placebo value for each medication night variable (i.e., 4 placebo values and 4 drug values) and that the repeated measures ANOVA had terms for overall drug versus placebo (1 df), night (1 df), and drug dose (1 df). Second, because the tasks were repeated during each day, a
term for time-of-task administration was also added to the ANOVA model. All differences described in the results for each test are statistically significant.

For the Addition Task, there was a significant Time of Test × Drug Dose × Condition interaction for number of correct additions [TDC F(2,38) = 3.60, p < .03]. The data can be seen in Figure 1. At the first morning test point, fewer correct additions were performed following the .25 mg dose as compared to the .125 mg dose and placebo. However, by the final test each day, more correct additions were completed following the .25 mg dose than the .125 mg dose, and more correct additions were done in each drug condition than after placebo. For incorrect additions, there was a significant Time × Condition interaction [TC F(2,119) = 3.52, p < .05]. There were significantly more incorrect additions performed after medication at the first testing point than after placebo.

On the Wilkinson Vigilance Task, there were four significant 2-way interactions for the Hit Rate variable. The Hit Rate data are presented in Figure 2. One significant interaction indicated that Hit Rate overall following the .125 mg dose was superior to that following placebo or the .25 mg dose [DC F(1,87) = 7.54, p < .01]. Also, performance after medication improved after the third medication night as compared to the first such that performance after both drug doses was better than placebo after that night [NC F(1,29) = 11.11, p < .01]. Performance following the .125 mg dose was significantly better than the .25 mg dose primarily at the third (afternoon) testing period [TD F(1,208) = 3.86, p < .05]. Finally, performance was better overall following placebo at the early morning test time while performance was better overall following triazolam at the final afternoon test time [TC F(2,20) = 7.06, p < .01]. For False Alarms on the vigilance task a three-way interaction [DNC F(1,29) = 6.31, p < .05] indicated that false alarms were reduced following the last medication night in the .25 mg condition as compared to both placebo and the first medication night.

No significant effects were found on the Short-term Memory test.

For the Multiple Sleep Latency Test (Figure 3), latencies to consolidated sleep (i.e., at least three consecutive epochs of Stage 1 sleep or one epoch of Stage 2 sleep) were increased after medication as compared to placebo [DC F[1,101] = 6.24, p < .05]. The interaction occurred because latencies were increased more after the .125 mg dose (9.5 vs 7.4 min) than after the .25 mg dose (8.9 vs 7.8 min). However, a significant Time × Condition interaction [TC F[1,127] = 4.12, p < .01] indicated that MSLT values were significantly longer than placebo in both medication conditions following the 1200, 1400, and 1600 naps (see Figure 3).

The mood scale data revealed that while there was no significant change in sleepiness as measured by the Stanford Sleepiness Scale, there was a significant overall decrease in fatigue as measured by the Profile of Mood States on the day following the use of triazolam 0.125 mg as compared to
placebo \( F(2, 20) = 3.48, p < .05 \); respective means for placebo, 0.125 mg, and 0.25 mg were 6.2, 5.2, and 5.6. There was also an increase in vigor in the 0.125 mg condition as compared to both placebo and the 0.25 mg dose \( F(6, 57) = 3.86, p < .01 \); respective means for third test day 2 for placebo, 0.125 mg, and 0.25 mg were 12.0, 15.2, and 13.5. A significant Time × Study Day × Condition interaction for the tension scale indicated that tension was reduced at the last test point following the final medication period in the \( .25 \) mg condition as compared to placebo \( F(6, 33) = 3.41, p < .05 \); respective means for the last test for placebo, 0.125 mg, and 0.25 mg were 6.3, 4.5, and 3.9. A significant Time × Night interaction for the confusion scale did not involve medication use.

**Discussion**

This study showed that patients with periodic leg movements during sleep and significant daytime sleepiness can have their nocturnal sleep improved by triazolam 0.125 mg and 0.25 mg. Those sleep changes included an increase in total sleep time, sleep efficiency, and Stage 2. While improvement in total sleep or sleep parameters was not as great as that seen in a study of clonazepam and temazepam (5), it is probably due to the fact that subjects in the current study normally slept better at night and did not report insomnia after treatment. Sleep efficiency in that study and the current study were comparable.

As seen in other studies of benzodiazepines (5), triazolam did not reduce the total number of leg jerks seen during the night. Overall brief EEG arousals were also not reduced by trazolam. It is possible that changes in leg movement patterns were not found because periodic leg movements have been shown to have significant within-individual nighttime variance resulting in low observation reliability (18: and \( r = .43, NS \) on the placebo week in the current study). This contention is strengthened somewhat by our recent finding that triazolam significantly reduces arousals in patients with central sleep apnea (18) because apnea has higher observation reliability (19). Inability to identify a large change in arousal pattern associated with the change in daytime function is difficult to explain based on sleep continuity theory. Lack of stronger findings implies that either the best arousal variable has not identified or that other sleep stage or medication effects helped to facilitate daytime function.

The improved sleep EEG parameters were strongly reflected in the subjective sleep reports on which patients reported a shorter sleep latency, fewer awakenings, deeper sleep, and improved sleep quality. In addition, participants reported significantly decreased fatigue and increased vigor throughout the day following use of triazolam 0.125 mg. There were also several objective indicators of increased daytime function following the use of triazolam 0.125 mg. Objective sleepiness, as measured by the MSLT, was decreased after both doses of medication. While nap latencies were not decreased as compared to placebo at any point following medication use, they were significantly increased at the final two afternoon test points. Similarly, for the addition and vigilance tasks, performance tended to be near placebo levels during early tests but proved to be significantly better than placebo at later testing points (Figures 1, 2, and 3). In general, performance was worse at the early morning testing point following the 0.25 mg dose as compared to the 0.125 mg dose and placebo, and this decrease resulted in a significant interaction in correct additions. These differences disappeared or reversed at later testing points and therefore indicate some residual hangover at 0730 from the 0.25 mg dose.

Together, these data suggest that acute administration of triazolam, particularly the 0.125 mg dose, in older individuals with periodic leg movements, can improve nocturnal sleep. The improved sleep resulted in improved ratings of sleep, increased vigor, increased objective alertness (MSLT), and increased performance on attention and vigilance tasks. Both daytime sleepiness and periodic leg movements are common in older individuals. The present data suggest that it is possible to reverse some of the daytime sleepiness on an acute basis with triazolam. Intermittent therapy of healthy older individuals with the 0.125 mg dose of triazolam may be effective in improving sleep and daytime function. However, this study did not attempt to access the possible interaction of triazolam with alcohol or other CNS active medications.

Periodic leg movements are poorly understood at a neurophysiological level. Therefore most treatment strategies have been symptomatic. Besides benzodiazepines, several classes of medications including various opiates (20) and neurotransmitter precursors (7,8,21-23) have been used clinically. Some reduction in leg movements has been reported with opioids (20) and L-Dopa (23,8) but not with L-tryptophan (8), clonidine (22), or baclofen (7). However, as both opioids and L-Dopa may have undesirable side effects, continued treatment of periodic leg movements with benzodiazepine medications is likely.

These data contradict the notion that CNS depressant medications are contraindicated in all patients with an objective finding of daytime sleepiness. Clearly, it is possible that periodic leg movements disturb sleep by fragmenting the underlying sleep process and that the fragmentation contributes to the observed daytime sleepiness. Unfortunately, the current analyses have not been able to identify strong physiological variables that can clearly account for the improved daytime function. Triazolam appeared to decrease that fragmentation in the early part of the night and thus may have reversed some of the sleepiness. In general, however, the overall increase in daytime nap latencies (from an average of 7.4 min to 10.2 min in the 0.125 mg condition) still leaves patients with some residual sleepiness. Significant improvement in daytime alertness and performance following the third night of medication as compared to the first night implies that some of the effects of improved sleep might be cumulative. However, periodic leg movements are usually considered to be a chronic problem. Further study is required to determine whether triazolam or other benzodiazepines maintain effectiveness in promoting both sleep and daytime function in these patients during chronic or repeated acute administration.
ACKNOWLEDGMENTS

This research was supported by The Upjohn Company and the Sleep-Wake Behavior Disorders Research Institute.

Address correspondence to Dr. Michael H. Bonnet, VA Hospital 111P, 5901 E. Seventh Street, Long Beach, CA 90822.

REFERENCES


Received May 26, 1989
Accepted September 19, 1989