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DRUG EFFECTS

In the previous section of this chapter, we described in considerable detail the role of alcohol in producing death, injury, and damage on the highway. The conclusions were obtained by combining results from both experimental studies on the effects of alcohol on behavior and epidemiological studies of alcohol presence in highway crashes. The U.S. government has for many years routinely gathered data on all fatal collisions in the United States, including the presence and level of alcohol. The federal government also gathers data from states to a lesser degree on non-fatal crashes, including reports on alcohol levels. This data, coupled with the more intensive epidemiological studies exemplified by the Grand Rapids Study (Borkenstein, et al., 1964) have permitted analysis of the relationship between BAC levels and increased crashes and injuries.

The key to analysis of the relationship of the BAC level and accident probability is the comparison of the BAC level in accident involved drivers with the BAC level in non-accident involved drivers on the same road at similar times. This comparison is possible because when we obtain either a breath or blood sample from a driver at a given time, the BAC level found in the breath or blood is an excellent representation of the BAC to be found in the brain of that driver, which in turn is determining his behavior. Alcohol is a unique drug that, when ingested and absorbed from the stomach and intestines, travels throughout the body rapidly, reaching an equilibrium in which the alcohol level is roughly equal in the water of any portion of the body. The mean adult male body consists of 58% water; the mean female body, 49% water. Less than 20% of this water is in the blood: the majority is distributed elsewhere throughout the body. Wherever we take a sample, whether from the water vapor of the breath, the urine, the blood or after death from various other portions of the body, we will find roughly the

same concentration of alcohol. Thus, whenever we determine the alcohol content of a body fluid sample, we have a good index of the alcohol level in the water of the brain, which is the ultimate determinant of the effect on behavior. This permits us to determine alcohol's influence on accident rates by comparing the level of alcohol in the samples taken from crash-involved drivers with that of controlled, non-crash-involved drivers. There is some variability in this relationship since it assumes that the alcohol has been completely distributed within the body, a process that takes time. There is additional variability in that the behavioral effects of a given BAC level are modified by factors such as the age of the driver and the quantity and frequency of his or her typical alcohol consumption. However, these factors are less significant in comparison to the magnitude of the effects of alcohol, especially for the levels above 50 mg/dl.

We present the above discussion on how knowledge regarding alcohol's effects on highway safety is derived to warn readers that there is no other such similar simple relationship between drug levels in body fluids and resulting behavioral changes. Obtaining blood or urine specimens from drivers and analyzing them for drugs does not necessarily shed light on the unknown drug levels in the brain that determine the behavior.

As an illustration consider marijuana and its prime active constituent, tetrahydrocannabinol (THC). Smoking marijuana cigarettes produces peak THC level in the blood within the first ten minutes of smoking. Within two hours after smoking, the THC level in the blood is at very low levels, typically below 5 ng/ml. After three to four hours, the level is so low that only very sensitive chemical analytical procedures are likely to pick it up. However, studies indicate behavioral effects for twelve or more hours in experimental laboratory studies. THC accumulates in fatty tissues in the body and dissipates slowly over an extended period so that its metabolite can be present in the urine for three weeks or more. Neither the blood level nor the urine level provide a simple relationship to the behavioral impairment found for marijuana. Nor do they clearly indicate what the levels are in the brain sites that determine the behavioral effects of marijuana. Based on the alcohol literature which relies heavily on blood alcohol levels to indicate behavioral effects, many readers may be misled into drawing conclusions about

the possible behavioral influence of a drug based simply on a blood, serum, or urine level report.

This problem makes it difficult to draw conclusions from epidemiological studies in which drugs are found in blood or urine samples taken from collision involved drivers. Moreover, we do not have comparative levels from non-collision involved drivers on the same road at the same time, since although we get cooperation requesting breath samples in alcohol studies, attempts to get blood or urine samples from volunteer drivers have been notably unsuccessful. Until technology improves, possibly with the use of new techniques to extract drug from saliva samples that control subjects might be more willing to contribute, attempts to compare drug levels in crash and non-crash involved drivers are not possible.

Moreover, as the above discussion suggests, having the drug levels from a body fluid sample in a collision involved driver merely indicates that the driver is a drug user. Suggestions as to how that drug level will relate to behavior must necessarily depend - at this point in history - primarily on laboratory experimental studies, clinical observations, and drug levels in patients who have expired from overdose.

One attempt to circumvent the difficulties in epidemiology resulting from the lack of a willing control group is the use of the concept of crash responsibility or culpability. For example, Williams, et al. (1985) obtained blood samples from 440 young California male drivers between the ages of 15 and 34 who died in motor vehicle crashes. 37% of the samples showed the presence of marijuana, 11% showed the presence of cocaine, and there were smaller frequencies of other drugs such as methamphetamines and diazepam. A confounding factor was the presence of alcohol in 70% of the fatalities, most typically in conjunction with the presence of other drugs. These figures at first flush appear highly suggestive, but no comparable control group was available. The authors resorted to examining the police report for each accident involved driver and attempting to assign culpability or responsibility for the crash. Drivers who had no drugs or alcohol present were found responsible for the crash 71% of the time. The presence of alcohol alone led to a 92% assignment of crash responsibility on average, ranging from 85% responsibility for drivers with below .10% BACs, to 96% with above .15% BACs. The presence of marijuana by itself in the body led to a crash responsibility percentage of 53%. Note that

this is less than the crash involvement responsibility figure for people with no drugs. On the other hand, drivers with marijuana in combination with alcohol were assigned responsibility for the crash 95% of the time. Drivers with marijuana present and BACs below .10% were assigned a 93% crash responsibility. Other drugs were present in insufficient frequencies to make statistically reliable assessments, except that collectively the presence of one or more drugs was associated with increased crash responsibilities over that of non-drug users.

A similar epidemiology study using crash culpability was performed by Terhune, et al. (1992) utilizing 1,882 fatally injured drivers for seven states. Alcohol was present in 51.5% of the drivers' bodies and other drugs in 17.8%. The most frequently reported drugs were marijuana, 6.7%; cocaine, 5.3%; benzodiazepines (tranquilizers), 2.9%; and amphetamines, 1.9%. The culpability/ responsibility analysis indicated that the presence of alcohol alone resulted in an increased number of drivers considered responsible for their crashes compared to drivers with no drugs or alcohol present. If any other drug was present with alcohol, the percentage of drivers considered responsible for crashes increased. However, there was an insufficient number of cases of drivers with a drug present but no alcohol present to permit statistical analysis.

The above studies by Williams, et al. (1985) and Terhune, et al. (1992) exhibited another difficulty in performing epidemiological studies on drug usage during driving. Namely, that the majority of crash involved drug users have combined the drugs with alcohol.

These conclusions are confirmed by a 1996 national household survey on drug abuse (Townsend, et al., 1998). The authors interviewed 11,847 drivers age 16 and above, and asked whether they drove within two hours of drug or alcohol use. 23% had driven with alcohol alone, 4% with alcohol and drugs simultaneously and only 1% with drugs alone. Thus 80% of drivers admitting drug use had utilized alcohol simultaneously. This is consistent with the two epidemiological studies of fatal drivers. The two hour time period selected for the questions was based on the belief that nearly all drugs to be discussed would be behaviorally active during that period. 3.7% of the drivers reported using marijuana, 1% cocaine, 1% tranquilizers, .8% stimulants, and .4% sedatives.

The conclusion from these epidemiology studies is that the problem of alcohol use remains dominant for traffic safety. However, the presence of other drugs in combination with alcohol exacerbates the probability of an accident. Finally, the presence of drugs alone occurs in such a small percentage of drivers that it is difficult to perform epidemiological studies by categories of drugs on the possible contribution to traffic impairment.

The studies above have emphasized non-medicinal drugs, primarily those likely to be used illicitly. An epidemiological study on medicinal drugs by Skegg, et al. (1979) examined the medical records of more than 43,000 patients in England over a two year period. Of these patients 57 were injured or killed while driving either cars, motorcycles, or bicycles. Using a matching procedure, 1,425 control patients were selected based on locality, gender, and age. Crash-involved drivers were found to have been 4.9 times as likely to be using a minor tranquilizer as were the controlled drivers. While other drugs were also over represented, the numbers involved were too small to reach statistical significance. There are, of course, problems with this type of control group. There may well be other characteristics of the accident-involved drivers, other than the use of tranquilizers, that contributed to their accident probability. Controlling for locality, age, and gender may not be sufficient to reveal all the factors that contribute to accident probability.

A study by Terhune and Fell (1982) examined the role of alcohol and drugs in non-fatal injured drivers receiving treatment in a single Rochester, New York hospital. Marijuana was found in 9.5% of the drivers, tranquilizers in 7.5%, sedative and hypnotics in 2.8%, cocaine in 2%, anti-convulsants in 2%, and other drugs in much smaller quantities. Alcohol was present in 25% of all the drivers, 51% of the marijuana users, 32% of the tranquilizer users, and 80% of the cocaine users. Comparing the frequency of culpability, drivers with alcohol were twice as likely to be responsible for their crashes as drug-free drivers. Drivers with only marijuana were more frequently responsible but not to a statistically significant level. On the other hand those with tranquilizers were less frequently involved in accidents but, again, not to a statistically significant level. It should be noted that the analysis was made utilizing 497 drivers from whom specimens were obtained, but an additional 311 drivers refused to supply a sample of their body

fluids for analysis. Driver cooperation again represents a limiting problem in performing epidemiological studies, especially with non-fatally injured individuals.

It is important to note that the reliability of culpability/responsibility analysis of crashes rests on the accuracy of the collected data and the conclusions drawn by police investigators. A study performed by Shinar, et al. (1983) compared the data collected and the conclusions drawn by two groups independently investigating the same accident – a multidisciplinary accident investigation team from a university and a police investigation. This study concluded that police investigations, at least in mid-west America in the 1970's, failed to note many important determinants of accident causation.

The discussion above has emphasized the difficulty in reaching conclusions from epidemiological studies of drug involvement in traffic accidents. This does not preclude the successful completion of epidemiological studies granted the availability of additional information about drivers. For example, Hemmelgran, et al. (1997) performed a study examining the relationship between benzodiazepine use and motor vehicle crash involvement in elderly drivers. The study was performed in Quebec, Canada. The province of Quebec has a universal health insurance system, including a computerized file on all prescription drug use by individuals 65 years of age or older. It was also possible to obtain information on age, gender, population density of residence, history of motor vehicle accident involvement in the preceding two years, use of other CNS drugs, and a measure of health status using a chronic disease score.

The authors identified 5,579 drivers age 67 to 84 who were involved in an injury-causing crash during the years from 1990 to 1993. For each of the crash-involved drivers, ten non-crash-involved drivers were selected from a pool of almost a quarter of a million drivers in the province in the same age grouping. A logistic regression analysis was performed, which permitted accounting for factors that differed between the accident and non-accident involved drivers. This study demonstrated an increased probability of involvement in a bodily injury crash with the use of long half-life benzodiazepines, especially in the first seven days after use. The initial increased accident rate was 45%, which declined after weeks of use to an average of mid 20%. On the other hand, short

half-life benzodiazepines showed no evidence of producing a significant increase in accident probability.

This study is notable for the large number of subjects and the degree of data available about these drivers, permitting a sensitive statistical analysis to discern the difference between the two classes of benzodiazepine in their effect on injury crashes. The magnitude of the increase in injury accident probability for the long half-life benzodiazepine is small in comparison to that produced by even moderate levels of alcohol.

The results suggest that there are epidemiological studies that can be performed analyzing drug effects on traffic safety but that performing such studies will be far more difficult and require more extensive information than was required for determining the influence of alcohol on traffic safety. While our discussion has emphasized the methodological problems involved in obtaining epidemiological data regarding drug effects on traffic safety, this should not be taken as a suggestion that there is not a likelihood that many CNS acting drugs do in fact increase the probability of highway collisions. There are two sources of information regarding drugs that have produced data suggesting traffic safety impairment by drugs. First, there is an extensive literature of thousands of experimental studies performed in the laboratory, in driving simulators, and in closed course driving that have demonstrated that many drugs, both illicit and medicinal, impair driving skills performance. Furthermore, there is considerable clinical evidence produced both by physicians and law enforcement that document serious deficits in drivers under the influence of drugs.

An example of the latter is a Norwegian study of amphetamines in drivers exhibiting impairment. (Gjerd, et al., 1992). This study reported on 380 individuals who were arrested for possible driving under the influence of drugs. Suspicion was aroused by collisions, overtly dangerous driving, stealing vehicles, and other criminal offenses. The study population was selected because toxicological studies all indicated the presence of amphetamines. In 79% of the cases, there was an additional drug present such as marijuana, opiates, and benzodiazepine. These drivers were subjected to sobriety testing and for those with only amphetamine present, 78% were evaluated as clinically impaired

for driving. 92% of the drivers had amphetamine levels beyond any levels produced by legitimate prescription use.

Logan (1996) reported on a study of 28 drivers who were either arrested or had been fatally injured in traffic accidents where toxicological evidence of methamphetamine was found. The 28 cases exhibited behavior such as leaving a lane of travel, crossing into opposing traffic, speeding, failure to stop at stop signs, and generally erratic driving. 82% of the blood samples recorded methamphetamine levels above any therapeutic level.

Both of these studies describe aberrant behaviors by drivers under the influence of either amphetamine or methamphetamine and support the inference that these substances produce dangerous driving behaviors. However, without adequate control drivers to serve as a comparison, it is impossible to estimate the magnitude of amphetamine effects on collision probability.

The more substantial literature of experimental studies, which have examined subjects administered drugs and tested under controlled conditions, have shown that many CNS active drugs produce substantial skills impairment. Many of these studies have examined multiple dose levels, acute versus chronic use and changes in skills performance as a function of time since initial drug ingestion. Reviews of the effects of drugs on driving related skills have been performed for benzodiazepines by Ellinwood and Heatherly (1985) and Linnoila and Seppala (1985); antihistamines by Starmer (1985); anti-psychotic drugs by Judd (1985); and marijuana by Moskowitz (1985).

Drawing conclusions about the effect of current medicinal drugs on skills performance important for driving or industrial work has to take into account that drug companies have in the last two decades exerted efforts to create new drug formulas with lessened side effects, especially with regard to driving. There have been notable improvements in curtailing the skills performance side effects of tranquilizers, antidepressants, and antihistamines. For example, in a recent review of antihistamines by Simons (1994), a contrast was drawn between the first generation of antihistamines, such as diphenhydramine and chlorpheniramine, and second generation antihistamines, such as terfenadine and cetirizine. The review of more than 250 experimental studies reported that first generation antihistamines frequently caused sleepiness and CNS dysfunctions,

including changes in reaction time, coordination, vigilance, arousal, performance in driving, EEG test, and sedation. The second-generation antihistamines, which are based on different chemical formulations, are designed to resist penetration into the central nervous system and have a lower affinity for side effects than the first generation. While the author concludes that there still exists no 100% risk-free antihistamine, the second-generation antihistamines, which, incidentally, vary among themselves in their CNS effect, have members that have not shown statistically significant differences from placebo on behavioral tests.

In conclusion, there appears sufficient evidence from laboratory experimental studies to delineate the many members of CNS active drugs that produce impairment of behavioral skills important for driving. The extent to which a specific drug user, using a specific quantity of drug is likely to be involved in an accident is much more difficult to determine. There are many psychoactive drugs, such as antihistamines, that uniformly carry warnings advising curtailed driving and specifically state that they are not to be used with alcohol. Clearly, if used with caution and with some sensitivity to symptoms of sedation, the evidence suggests that the probability of accident involvement would not be great. Currently, there have only been a few epidemiological studies examining antihistamines' effects on accident probability, and these have not produced much information. Given the small magnitude of effects by second generation antihistamines in skills performance studies, it would be expected that epidemiological studies would have difficulty finding such effects. To obtain statistically significant effects for a drug influence, the magnitude of that influence has to rise above the variability of accident rates in the population. On the other hand, as noted from the two studies on amphetamines and methamphetamines described earlier, when individuals are using drugs primarily as an illicit substance, taking doses far beyond the normal medicinal levels, it is not surprising that there should be police and clinical reports of substantial impairment and involvement in traffic collisions. Thus, decisions about how serious a menace to traffic safety a given drug is must rely on a function of the number of people utilizing the drug and the levels at which they are used. Surveys in recent years demonstrate that there is a sizable fraction of the population that drives with marijuana, cocaine, or methamphetamines. Given the problems of performing epidemiological

studies, there remains no definitive evaluation of how serious the problem is on the road with regard to these drugs. I speak now in terms of the seriousness of the problem as an overall public health problem. If only 500 people in the country used methamphetamine at a very high level and were grossly impaired, this would still be merely a statistical blip among the vast millions of traffic collisions that occur annually in the United States.

On an individual crash basis, if you are the unlucky victim of an individual under the influence of a drug, limited epidemiological knowledge may offer little solace. Your only recourse with respect to possible civil redress is to look at the experimental literature, the clinical reports regarding behavior and overdoses, and finally the very nature of the crash incident, which suggests the character of the deficits. It would, however, be impossible to resort to the widespread specific knowledge that has been generated with regard to alcohol use in your case.

It should be noted that interest in the influence of alcohol on traffic safety was expressed more than 100 years ago and that serious research with regard to behavioral effects of alcohol on skills performance were performed as early as the second decade of the 20th century. That research accelerated with the development of more accurate methods for determining the level of alcohol in subjects, and each decade has seen a substantial increase in the number of studies in the alcohol area. By comparison, we are at a much earlier stage in our research on drugs, especially with regard to epidemiological studies