Abstract

This report reviews evidence which has been obtained in Australasia and elsewhere concerning the roles of drugs (prescription, over-the-counter and illicit) in traffic violations and crashes. The appropriateness of alcohol as a model for the study of the effects of other drugs on driving behaviour and traffic safety is discussed.

Keywords

DRUGS, DRIVING, LITERATURE REVIEW

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Federal Office of Road Safety

Drugs and Traffic Safety

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SUMMARY

It appears reasonable to conclude that some drugs have the potential for impairing human psychomotor skills which are relevant to driving and some fragmented pieces of evidence suggest that drug-induced impairment of driver performance constitutes a traffic safety problem.

Possible countermeasures might include a requirement by the drug regulatory agencies for the generation of information on the behavioural toxicology (adverse effects on human skills performance) of new drugs before marketing. This should include, at the very least, an indication of the effects of the drug across the projected therapeutic dose range, both alone and when combined with "social" amounts of alcohol. Such information could then be disseminated to health professionals and the general public so that the appropriate choice of medication could be encouraged and information/warnings made available.

The laws for driving under the influence of drugs are considered by some to be inadequate and open to improvement. It is to be hoped that new epidemiological findings, together with more objective methods of assessing driver intoxication, may provide a more rational basis for the control of drug-impaired driving. This is especially important where driving has been affected by the use of illicit euphoriant or by the recreational use of prescription drugs.

In the long term, however, the development of less-impairing prescription drugs by the Pharmaceutical Industry and the enthusiastic marketing of these is most likely to improve the situation. There are signs that this process has begun with the new histamine H1-antagonists (antihistamines), for example, which are considerably less sedating than their older counterparts.

An important priority is to establish the extent and nature of drug use and abuse among drivers. Then the findings for drugs in compromised populations of drivers can be put into context and the design of any new studies which might be envisaged can be optimised. This is the objective of the current Federal Office of Road Safety Research Programme on Drugs and Driving.
Introduction

Driving a motor vehicle is a complex multifunctional task involving visual search and recognition, vigilance, information processing under variable demand, decision-making, risk-taking and enough sensorimotor control to carry out all these activities correctly (Willette & Walsh, 1983). It is also an overlearned (where practice has obviated the need for conscious recall) task, where critical high level demands are very infrequent.

Impairment of driving performance has been defined (Consensus Report, 1985), in a general sense, as the failure to exercise the expected degree of prudence or control to ensure safe operation of the vehicle under the traffic conditions pertaining at the time. This is often expressed as traffic violations and traffic crashes. Such alterations of behaviour are not specific to drugs, however, and can be associated with distraction, emotional stability, aggression, fatigue, physical illness, psychiatric illness and many other factors which can show complex interactions. Della-Glustina (1977) also pointed to the complex interactions of age, chronic disease and prescription use as well as non-medical factors in traffic accidents and considered that traffic education, including the use of simulators in rehabilitation programmes for culpable drivers might provide an improvement of the status quo.

The medical and social costs of traffic accidents to the community are immense. Transport accidents in 1988 were conservatively estimated to have cost Australian society $6.6 billion. Road accidents contributed $6.1 billion (94%) to this total. Aviation accidents cost $64 million (1%), rail $94 million (1.4%) and maritime $264 million (4%) (Bureau of Transport and Communications Economics, 1992). Although road crashes are
responsible for just over 2% of total deaths in Australia each year, they account for almost 7% of years of life lost through all causes of death. This is more than the years lost through cerebrovascular disease and cancer. When only years of life lost during the working age span are considered, road accidents account for more years lost than through all forms of heart disease and about 75% of those lost through all cancers (Federal Office of Road Safety, 1991). The Federal Office of Road Safety Road Fatality Statistics for 1990 indicate that there were 2328 fatalities in Australia in that year and about ten times that number of serious injuries. Each fatality costs the Australian community $300,000, in 1985 terms, and each serious injury $52,000.

The relationship between alcohol and increased traffic violation rate and an increased crash risk is now well-established. The first recommendation for mandatory alcohol testing for crash-involved drivers was by Widmark in 1914. Because of this, many alcohol countermeasures have been put in place and the extent of enforcement is now the main criterion of success. With the introduction of per se drink-drive legislation, where the perceived risk of apprehension has been greatly increased, and of community awareness and education programmes, alcohol-related accidents have begun to decline.

A number of drugs have central nervous system effects which are remarkably similar to those of alcohol. Like alcohol, these drugs are subject to the development of tolerance (with continued use of the drug, there is a need to use increasing doses to reproduce the initial effect) and often demonstrate cross-tolerance (the extension of tolerance acquired to one drug to a second drug) with alcohol. It would be surprising if such
drugs did not have a similar potential to influence behaviour. Nevertheless, concern that drugs other than alcohol might be important in traffic safety has only recently been expressed. Even more recently, epidemiological studies have begun to identify many prescription and over-the-counter drugs as being over-represented in drivers who are killed or injured in traffic accidents. Information on the behavioural toxicology (which, in this context, includes the adverse effects of the drug on human skills performance, such as the ability to drive a motor vehicle, operate machinery or work in a hazardous environment) of these drugs is scant. Most of the drugs so identified have the ability to impair driving-related skills. Thus, although a massive campaign has been organised to counter the detrimental effects of alcohol on driving, the results of drugs-driving research have been claimed to be mostly of academic interest and to have little significance in licensing and regulatory terms (Irving, 1986). This may be because therapeutic drugs taken for legitimate therapeutic purposes are tacitly assumed to restore driver ability towards normal. This may or may not be the case (de Gier et al., 1986; Gerhard & Hobi, 1986).

In this paper, evidence which has been obtained in Australasia and elsewhere concerning the roles of drugs (prescription, over-the-counter and illicit) in traffic violations and crashes will be reviewed. The results of the Australian studies have been examined in greater depth for obvious reasons. Before this, the appropriateness of alcohol as a model for the study of the effects of other drugs on driving behaviour and traffic safety will be discussed.
Lines of evidence which suggest the existence of a drugs-traffic safety problem.

At present there are a number of fragmented lines of evidence (Starmer et al., 1988) which support the hypothesis that drug-induced impairment of driver performance constitutes a traffic safety problem. No real estimate can yet be made of the magnitude of this problem. The lines of evidence are:

1. The intrinsically impairing properties of a large number of drugs (prescribed, bought over-the-counter and recreational).

2. The ability of certain drugs to exacerbate the effects of alcohol.

3. The widespread use of these potentially impairing drugs in the community, including driver, as indicated by the results of surveys (e.g. Reynolds et al., 1977; Hendtlass, 1983).

4. Evidence from prospective surveys, such as that carried out by Skegg et al. (1979), where it was shown that there was a highly significant association between the prescription of minor tranquillisers and the risk of a serious road accident.

5. The apparent over-representation of the same drugs in drivers who are killed on the roads, who present at hospital as the result of a crash or who are apprehended by police for aberrant driving behaviour.
Drug and alcohol usage in Australia

There are a number of aspects of the drugs and traffic safety problem which appear to be almost uniquely Australian. For its size, Australia has a very small population. There is also a very high degree of urbanisation in Australia with approximately 84% of the population living in the cities which are widely separated (average distance apart of State capitals is 2234 km). Away from the cities, the majority of roads are lightly trafficked and there is a high proportion of unsealed roads. The frequency of vehicle ownership is high in Australia and both the road crash mortality and casualty rates are also high (Australian Bureau of Statistics, 1985; Federal Office of Road Safety, 1986).

Estimates of prescription drug usage can be obtained from the National Health Service (Pharmaceutical Benefits Scheme) and other audits. Of the 250 most frequently-prescribed drugs, about 25% are either known or suspected to be capable of impairing human skills performance.

By any standards, the frequency of drug usage in Australia is high (Stolz, 1978). It was reported by Webb (1982) that 8.9 prescriptions were dispensed per adult in 1981 and that about 20% of these prescriptions were for central nervous system-active drugs. This compares with only 5-6 in the U.S.A. (Wade, 1976). It was found that 54.6% of Australian adults had taken some form of medication in the 2 days prior to the survey (Australian Bureau of Statistics, 1979).

Alcohol usage in Australia is also high compared with that in many other countries (Brown et al., 1982), Australians being stated to consume 10.2
litres of alcohol per year compared with only 7.3 litres per year by the British.

The drinking and drug-taking (sedatives, tranquillisers, antidepressants) patterns of 14,500 adults (aged 26 - 65) who attended a Sydney health testing facility was surveyed by Reynolds et al. (1977). It was found that significantly more females (16.1%) took these drugs regularly than males (6.7%). Heavy drinking appeared to be predominantly a male phenomenon but drinking was not a substitute for drug-taking and the ones who drank every day were those who reported most frequent drug use. More recently, however, a group of females with a high alcohol usage pattern, resembling that of males, has been identified in New South Wales (Spragg, E. - personal communication, 1989). The use of illicit drugs, particularly cannabis in the 18-30 age group, is also widespread in both Australia (Chesher et al., 1986) and New Zealand (Casswell & Hood, 1977).

**Drug usage by drivers**

The question to be answered is whether prescription and over-the-counter drug usage in the driving population (after suitable adjustment for age and sex) reflects that in the population at large. This has never been established in Australia and is the subject of a current Federal Office of Road Safety research initiative. Then it is necessary to know whether modifications of these patterns occur in those who commit traffic offences or who are injured in traffic crashes. It is also important that the extent of the recreational use of prescription drugs and illicit substances be established. The evidence for this will now be reviewed but it is important to note that the last time this literature was comprehensively reviewed was
more than a decade ago (Veldkamp et al. 1980).

Since prescribing patterns are known to vary with time and place (Bergman & Sjoqvist, 1982) and illicit drug usage can similarly change according to local fashions and opportunities (Editorial, 1985; Mclean et al., 1985), it is important that local surveillance efforts be initiated and maintained.

The suitability of alcohol as a model for the study of the effects of a drug on driving behaviour and traffic safety.

The relationship between the consumption of one drug, alcohol, and increased traffic violation rate and an increased crash-risk is well established. As stated earlier, the first proposal that mandatory blood alcohol tests should be imposed on crash-involved drivers was made by Widmark in 1914. Since that time, epidemiological, laboratory and on-road studies have consistently supported this direct causal relationship. The risk of a driver being involved in a road accident increases exponentially as the blood alcohol concentration increases (Perrine, 1975). The more serious the incident, the more likely is alcohol-involvement to be found. In the U.S.A., drivers who had consumed alcohol were 49% more likely to be killed in a road accident than those who had not (MMWR Report, 1982). Alcohol-involvement in road fatalities has been reported at 69.2% for drivers (Ito et al., 1983) and 66% for motorcyclists (Larsen & Hardt-Madsen, 1987). In injured cyclists, the prevalence of alcohol was found to be 25% (Luna et al., 1984) and in injured moped operators, 14% (McHugh & Stinson, 1984).

Alcohol contributed to about 36% of driver and motorcycle fatalities
occurring in Australia during 1991 (Federal Office of Road Safety, 1991). One in three of those drivers killed on the road and one in five of those who were injured had a blood alcohol concentration equal to or greater than 0.0591100 ml (Johnston, 1982). Road accidents were stated to be the predominant cause of neurotrauma in New South Wales and 50% of drivers dying from such injuries have been found to have high blood alcohol levels (Selecki et al., 1981).

Alcohol-involvement is not uniform across the population. Of those drivers injured in crashes, males were much more likely (36%) to have consumed alcohol than their female (12%) counterparts (McDermott & Hughes, 1983).

Young drivers are invariably over-represented in road accidents, including alcohol-related accidents. The blood alcohol concentrations of these drivers are often very low. A greatly increased crash risk at low blood alcohol levels may be a function of young drivers having less alcohol tolerance and less driving experience than more mature drivers (Council Report, 1986). In Victoria, drivers with probationary licences had a tripled risk of road accident injury compared with those with full licences. Most states in the U.S.A. have raised the minimum drinking age to 21 which has resulted in a 13% reduction of traffic crash fatalities in young drivers (Dumouchel et al., 1987).

With the general recognition that alcohol is a major contributor to serious road accidents, a wide range of countermeasures has been implemented. Some of these, such as the massive random breath testing campaign in New South Wales, have been dramatically successful (Homel, et al.,
1988). This success relates largely to the fact that alcohol is an easy drug to detect and quantify. Large doses (tens of grams) of alcohol are needed to produce discernible alterations of driving-related behaviour and alcohol is dealt with by the body in a very simple manner. Since a proportion of an alcohol dose is eliminated in expired air and since deep lung air is in equilibrium with arterial blood, breath analysis can give a rapid and accurate estimate of the blood alcohol concentration at a very low cost, without the need to resort to invasive sampling. This has greatly facilitated the enforcement of drink-drive legislation and with the concomitant introduction of community awareness and education programmes, driver behaviour has been altered and alcohol-related traffic accidents have begun to decline. The development of passive breath alcohol sampling has greatly speeded roadside testing and has increased the detection rate for drunk drivers from 45% to 70% (Jones, 1986).

Some other suggested countermeasures have been the use of a critical tracking task to serve as a drunk driver warning system (Bodi et al., 1986), breath analysis interlocks (Breakspere & Porter, 1987), reliable means of self-testing (Breakspere et al., 1987) and the use of horizontal gaze nystagmus as a roadside method of detecting alcohol intoxication at the roadside (McCamey, 1986). Server (bar staff) intervention programmes have been introduced in the U.S.A. to decrease the likelihood of a bar patron leaving the premises in an intoxicated state (Rus & Geller, 1987).

Thus, for a variety of reasons, which relate to dosage, pharmacokinetics (which describes quantitatively the rates of the various steps of drug disposition), metabolism and elimination, alcohol has provided an unusually good model for studying the effects of a drug on driving performance but
other drugs of concern do not share these characteristics. (Consensus Report, 1985).

There has developed an understandable but regrettable tendency to separate alcohol from other impairing agents and at the same time to enact tough drugs driving legislation which remains firmly based on experience with alcohol. This is illogical, inappropriate and usually quite unenforceable. There is often pressure to define, for legal purposes, critical body fluid concentrations above which all would be impaired and below which no impairment would be demonstrable. At present, although desirable, this is not possible. In addition to the considerably more complex pharmacodynamic (biochemical and physiological effects of the drug and its mechanisms of action) and pharmacokinetic profiles of most drugs compared with alcohol, there is always the proposition that therapeutic drugs, used for legitimate purposes, may improve the driving ability of certain patients, despite their potential to impair the performance of normal individuals. This is not so for alcohol and recent evidence suggests that there is no threshold for alcohol-induced impairment (Moskowitz & Robinson, 1988).

Cannabis and driving impairment

Cannabis, the other widely-used social euphoriant, can also impair driving performance. Rood (1979) reviewed studies which have examined the effects of cannabis on driving. It was concluded that cannabis impairs visual perceptual performance to a large degree. There is a statistically significant impairment of colour discrimination, an initial impairment of the ability to sustain attention, which deteriorates further over time, a failure to
detect random stimuli (especially if additional central processing is required) and a dose-dependent failure to detect stimuli in the periphery. Pursuit tracking tasks are impaired by cannabis. Visual autokinetic motion increases in a dose-dependent manner, which is said to present a night-driving hazard. Cannabis does not apparently increase aggression and risk-taking behaviour. The interaction of cannabis and alcohol on driving performance has generally been found to be additive (Attwood et al., 1983).

**Drug-alcohol interactions**

Many drugs interact with alcohol to exacerbate alcohol-induced impairment. These drug-alcohol interactions may be absorptive and/or metabolic in nature and are usually either additive or synergistic. Alcohol is usually, but not always, the dominant partner in the interaction. Drugs rarely antagonise the effects of alcohol and when they do, the pattern of antagonism is incomplete. Table 1 lists the questions which must be resolved before the nature of a drug-alcohol interaction can be assessed.

**Table 1. Questions to be resolved before the nature of a drug-alcohol interaction can be assessed (Starmer & Bird, 1984).**

<p>| | |</p>
<table>
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<tbody>
<tr>
<td>1</td>
<td>Is the time to peak effect of either alcohol or the drug altered in the presence of the other?</td>
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<td>2</td>
<td>Does the magnitude of the peak concentration change for either the drug or alcohol in the presence of the other?</td>
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<tr>
<td>3</td>
<td>Do the observed effects parallel the blood concentration of either the drug or alcohol?</td>
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<tr>
<td>4</td>
<td>Are the dose-response curves for either drug or alcohol altered in the presence of the other?</td>
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<tr>
<td>5</td>
<td>Is the nature of the interaction consistent with several different dose ratios?</td>
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Issues concerning drugs and driving impairment

The World Health Organisation (Willette & Walsh, 1983) has stated that a priority in traffic accident research should be given to develop methods for determining the degree to which driving performance is impaired as a consequence of a driver having taken a drug. The World Health Organisation recognised that conflicting evidence concerning the effects of both licit and illicit drugs on human performance is to be found in the literature. This is mainly because of a failure to relate the extent of impairment to the concentrations of drugs and their active metabolites in body fluids, poor methodology and inappropriate tests. Very little information is available concerning the behavioural toxicology of many of the drugs which have been identified in epidemiological studies as contributing to road crashes. Except for alcohol, there is very little empirical data which closely defines the relationship between the concentration of a drug in body fluids and the behavioural effects which occur. Even then, factors such as acute and chronic tolerance obscure the issue.

Apart from carrying out epidemiological surveys, it was recommended by the World Health Organisation (Willette & Walsh, 1983) that systematic test procedures for assessing prescription drugs as potential traffic safety hazards be developed. The precise way in which these functions were tested was considered to be unimportant, as long as the tests were capable of revealing impairment relative to traffic safety induced by reference drugs (e.g. alcohol, diazepam and pentobarbitone) in a dose-related manner. At the very least, prescription drugs, which are widely used should be examined in order to establish a profile of their effects on
human psychomotor performance. Priority should be given to those drugs which are known or suspected of being able to impair driving performance and to increase crash-risk. The drugs should be given acutely in several doses across the therapeutic range and also sub-chronically, to determine whether tolerance and/or cumulation occurs. The interactive effects of the drugs with alcohol should also be investigated and the mechanism(s) which are operative should be established. This information should represent a minimum requirement for the registration of new drugs and for the continuation of the licence of many established drugs. At present, there is no requirement that the behavioural toxicology of new drugs be evaluated before marketing but this has been strongly recommended (Haller et al., 1986). Such proposals are under active consideration by the Food and Drug Agency in the United States and the European Pharmacopoeia Commission. It has also been recommended that the medical profession make the public more aware of the detrimental effects of some drugs on driving performance (de Gier, 1981) but little real progress has yet been made.

"Although the relationship between drug dose and impairment provides useful information, it is much more important that attempts should be made to establish dose-response profiles across time. Pharmacokinetic/pharmacodynamic modelling should be used to explore any correlations which may exist between the concentrations of drugs and their metabolites in plasma and the extent of impairment. An attempt should also be made to determine whether a plasma "threshold" concentration for significant impairment can be established. Also it should be determined whether individual differences in dose-response can be partly (or even largely) explained as different blood levels or whether
differences exist in the level of response to similar blood levels.

Both prescription and illegal drugs are used for purposes which bear little relationship to normal therapeutic indications or intent. This has ramifications into traffic safety. Not surprisingly, a wide variety of user groups has been identified. For example, Vanoonberbee (1982) found that unemployed persons who were stopped for driving under the influence of alcohol had higher blood alcohol levels than other groups and they reported drinking more frequently and taking more prescription drugs.

The possible interaction of medical conditions and medications in their effects on driving ability.

It is clear that many medical and psychiatric conditions can adversely affect driving ability. It is possible that with the appropriate use of drugs the patient's driving ability may be restored towards normal. This proposition should not be taken for granted, however. Clinical depression is associated with a reduction in driving ability. Tricyclic antidepressants, which are intrinsically sedative in nature and cause driving impairment in normal individuals, will improve the driving ability of depressed patients (M. Linnoila - personal communication, 1992). Clinically anxious patients are also poor drivers but although treatment with benzodiazepine tranquillisers will improve their clinical condition there is no improvement in their driving ability (De Gier et al., 1986).

Further insight into the difficulties in separating the effects of drugs on driving ability from those of the medical conditions which they are used to treat can be gained from a study (Deasy & Ramsay, 1984) which
investigated a possible relationship between antihypertensive treatment (and other relevant variables) and road traffic accidents. Each member of a cohort of hypertensive patients (n = 49) who had been involved in a road crash was matched with a non-crash case on age, sex and miles driven per week. No association was found between traffic crashes and the severity of the clinical condition or with the use of psychotropic drugs, alcohol, antihypertensive treatment (in general), b-adrenoceptor antagonists or central nervous system drugs. Crash incidence was found to be positively associated (6.7-fold increase; p < 0.05) with the use of adrenergic neurone blockers (guanethidine, bethanidine and, particularly, debrisoquine). The Framingham study also addressed this problem but could find no such relationship (Farmer et al., 1990).

Guidelines (Starmer, 1988) which may be used to make an assessment of the relative importance of a particular drug or drug group as a potential traffic hazard are listed in Table 2.

**Table 2. Guidelines for the assessment of the hazards to traffic associated with the use of a drug or group of drugs (Starmer, 1988).**

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<table>
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<tbody>
<tr>
<td>(1)</td>
<td>Does the drug have effects which may impair human skills performance?</td>
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<td>(2)</td>
<td>If so, what is the nature of the effects which occur?</td>
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<tr>
<td>(3)</td>
<td>Are these effects manifest at therapeutic dosage?</td>
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<tr>
<td>(4)</td>
<td>Do these effects occur in all or only in certain individuals?</td>
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<tr>
<td>(5)</td>
<td>What conditions is the drug used to treat?</td>
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<tr>
<td>(6)</td>
<td>Is the drug available only on medical prescription?</td>
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<tr>
<td>(7)</td>
<td>Is the drug used recreationally?</td>
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<tr>
<td>(8)</td>
<td>Does the drug interact adversely with other drugs or with alcohol?</td>
</tr>
<tr>
<td>(9)</td>
<td>To what extent is the drug used by the driving population?</td>
</tr>
<tr>
<td>(10)</td>
<td>Can the drug be detected in body fluids?</td>
</tr>
<tr>
<td>(11)</td>
<td>How often is the drug detected (or self-reported) in:</td>
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<tr>
<td></td>
<td>(a) Drivers apprehended by police?</td>
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<tr>
<td></td>
<td>(b) Drivers hospitalised after a crash?</td>
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<tr>
<td></td>
<td>(c) Autopsy samples from crash victims?</td>
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<tr>
<td>(12)</td>
<td>Is there reliable information linking the blood concentration of a drug with the expected degree of impairment?</td>
</tr>
<tr>
<td>(13)</td>
<td>Can a case be advanced that a driver is safer with his medication than without it?</td>
</tr>
<tr>
<td>(14)</td>
<td>Is the drug representative of its class and are alternatives available?</td>
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Evidence for the involvement of drugs other than alcohol in traffic violations and traffic crashes.

The influence of drugs, alone and in combination with alcohol, on traffic safety has been studied using both epidemiological and behavioural techniques. The results which have been obtained are reviewed below.

1. Epidemiological Studies

Epidemiological studies on drug use by drivers can be carried out by questionnaire and/or by the analysis of body fluid samples. The former method permits the use of larger populations but depends on accurate and truthful self-report. The latter method is limited by cost and the sensitivity and specificity of the assay methods.

Attempts to combine the two approaches (Finkle et al., 1968; Sterling-Smith, 1975) have required considerable resources of manpower and equipment and access to police, medical, social and legal records. It has been stated (McLean et al., 1985) that drugs-driving studies are very much "the art of the possible" as regards permitted sampling procedures and acquisition of data on driver and crash variables.

1a. Self-Report surveys

Several roadside surveys have been conducted in Australia. Hendtlass (1983) surveyed drivers stopped at random breath test stations in Melbourne (n = 3503), rural Victoria (n = 301) and Belfast, Northern Ireland (n = 1987). The results indicated that alcohol had been used by
5.3% of the Melbourne drivers, 2.1% of the rural Victorian drivers and only 1.5% of the Belfast drivers. Admitted drug use was 8.4% by Melbourne drivers, 2.6% for Victorian rural and 5.5% for Belfast drivers. Prescribed drugs were more frequently nominated than over-the-counter drugs. Several methodological difficulties existed in the study, arising from the self-report basis. The survey was biased against admission of illicit drugs and did not record sleeping medication taken the night before.

In an earlier study, Teo et al., (1975) found that 25% of a random sample (n = 10,000) of drivers who were breathalysed in New South Wales during 1972-73 admitted to have been taking drugs. MacPherson, et al. (1984) found that diazepam, oxazepam, CNS depressants, analgesics and drugs used for the treatment of diabetes were associated with an increased crash-risk, while Perl et al. (1985) found that minor tranquillisers and β-adrenoceptor antagonists were also associated with an increased crash-risk and culpability. Very few drivers admitted to illicit drug use in a survey reported by Perl et al. (1987), which is not surprising since the data were collected by police. The distribution of reported drugs was antidiabetics (2%), cardiovascular (12%), antibiotics (15.4%), analgesics (8.2%), CNS drugs (16.3%), anti-asthmatics (11.2%) and drugs for respiratory disorders (8%).
1b. **Analysis of body fluid samples**

Only in the last half of this decade have methods of chemical analysis been developed which are sensitive enough to cover the range of drugs which may be present in body fluids, often at very low concentration. In the past, high sensitivity analysis was achieved by optimising detection of a specific compound or group of compounds at the expense of other compounds. This is reflected in the earlier epidemiological studies which targeted mainly on illicit drugs or the sedative-hypnotics (Garriott & Latman, 1976).

Chromatography, mass spectrometry and immunoassay are methods used for the detection of drugs in body fluids. Immunoassay, although providing high sensitivity for specific compounds has limited use in drug screening programmes because only one drug at a time can be detected. Although chromatographic techniques are useful in screening, ultimately mass spectrometry is required for confirmation of drug identity. Gas chromatography-mass spectrometry becomes less effective as the range of drugs to be detected increases and samples become more complex.

In recent years a new generation of mass spectrometer, the triple stage quadrupole mass spectrometer (TSQ) has been developed and has shown high sophistication in rapid screening procedures (Brotherton & Yost, 1983; Hunt et al., 1985). Chemical noise can be reduced to such an extent by the TSQ that samples may be analysed directly without prior chromatography. The combination of capillary column gas chromatography with a TSQ mass spectrometer allows several hundred compounds to be detected in a single sample.
The success of this method is apparent in the number and range of positive drug detections found in an epidemiological study on crash-involved drivers carried out in the Department of Pharmacy at the University of Sydney as a joint project with the Roads and Traffic Authority of New South Wales. Up to 7 drugs were detected in a single blood sample. Drugs found in the blood of crash-involved drivers (other than alcohol, caffeine and the nicotine metabolite, cotinine) included hypnotics, cannabis, analgesics, b-adrenoceptor antagonists (and a b-agonist), anti-convulsants, minor tranquillisers, anti-histamines, non-steroidal anti-inflammatories, anti-depressants, narcotic analgesics, anorexics and both licit and illicit stimulants. Of the 824 samples which have been analysed, 439 (53.3%) were free of alcohol or drugs, 68 (8.3%) samples contained alcohol alone, 285 (34.6%) contained drugs alone and 32 (3.9%) contained alcohol plus drugs. Driver and crash variables were also recorded and the patterns in the relationships between these variables and the drug groups found and are currently being explored by correspondence analysis.

Drug usage (other than alcohol) by compromised motor vehicle drivers has consistently been found to be high, although the patterns of drug use have varied widely according to the time of the study, its location and the methodology employed. Where only apprehended and alcohol-negative drivers were studied, the extent of drug usage has usually been very high. For example, in the U.S.A., Finkle (1969) found a 25% drug incidence (273 different drugs) in drivers who were arrested for driving under the influence of alcohol. This proportion rose to 60 - 70% in a very large (n = 72,000) population of Californian drivers who were arrested for impaired driving but whose breath alcohol concentrations were too low to explain the observed symptoms (White et al., 1981). Also in California, Williams
et al. (1985) found one or more drugs in 81% of male drivers (n = 440) who were killed in road crashes. Two or more drugs were detected in 43% of cases.

In Germany, Moller et al., (1981) examined a series (n = 453) of samples from 3492 drivers who were suspected of driving under the influence of alcohol and/or drugs. Of these, 17.9% were drug-positive with only 17.6% in the accepted therapeutic range. Wilson (1985) found that 53% of samples contained prescription drugs in high concentrations while McLinden (1986) has found low concentrations of oxazepam (0.2 mg/l) in young drivers to be grossly impairing. This drug was used for recreational purposes and the drug concentrations found to be associated with overt intoxication are far lower than those in the clinical literature.

Missen et al. (1978) examined blood samples taken from New Zealand drivers (n = 1,000) who were hospitalised after a road crash for the presence of diazepam and alcohol. Alcohol was found in 93% and diazepam in 2% of cases. Evidence was found (by examining the ratio of the concentration of diazepam to that of its metabolite, N-desmethylidiazepam) for occasional recreational use in one third of the diazepam-positive samples. Diazepam alone or in combination with alcohol was considered to have caused impairment of driving ability in the majority of these cases.

An increase in the proportion of drug-positive cases has often appeared to parallel the severity of the situation in which the driver was involved. For example, Ulrich et al. (1984) reported that in a population of Swiss traffic accident victims (n = 144), 34.7% had measurable concentrations of
drugs. In a sample (n = 250) of traffic offenders, however, the incidence of drug-positive cases fell to 22.4%. Polydrug use was prominent in the study of Bailey (1985), who examined 289 consecutive emergency-room patients who were affected by alcohol. In half of these cases, comprehensive drug screening revealed the additional use of one to four other drugs including barbiturates, stimulants and narcotic analgesics.

Patterns of drug usage relate to the population studied, the location of the study and the time at which it was carried out. Some examples serve to illustrate the disparity of the findings.

Age-related differences in the patterns of drug usage have been reported by Bjorneboe et al. (1987). Toluene (an abused solvent) was most frequently found in drivers under 20 years of age, while D9-tetrahydrocannabinol (THC), the active principle of cannabis, was found to have been used by drivers in the 20 - 24 age group. Amphetamine, diazepam, flunitrazepam and morphine were more likely to be found in drivers over 25 years of age.

The incidence of cocaine in a Los Angeles County series of fatally injured drivers was 8% (Budd et al., 1989). Other drugs detected included: alcohol (41.5%), cannabis (19%) and barbiturates and phencyclidine (< 2%). In New York, Marzuk et al., (1990) reported a cocaine incidence of 18.2% and 10% of samples were also positive for cocaine and alcohol.

Special cases still apply. Clark et al. (1985) reported a major role for alcohol and only a minor role for drugs in the deaths of U.S. military personnel in traffic crashes but conceded that this may have been the
The range of prescription drugs taken by drivers also varies from place to place and from time to time, according to prescribing fashions. Illicit drug usage depends on cost and availability. Benzodiazepine derivatives are the most commonly detected drugs in blood and urine samples taken from Northern European drivers (Holmgren et al., 1985). Setekleiv, et al. (1980) reported that benzodiazepines were found in the blood of 7.3% of road accident victims. When all (road, industrial, home, leisure, drowning) accident victims were examined the incidence of benzodiazepines rose to 66.7%. Bjorneboe et al. (1987) examined blood and urine samples taken from Norwegian drivers who were apprehended on suspicion of driving under the influence of alcohol or drugs. The study looked mainly at drugs of abuse and found 45% of samples contained D9-tetrahydrocannabinol (THC), 37% contained diazepam and amphetamine was found in 23% of cases. It was found that only 36% of samples contained diazepam alone. Diazepam was found in combination with THC (34%) and amphetamine (21%). In Northern Ireland, drivers who came to the attention of police for impaired driving but who were found to be under the limit for alcohol, 18% of driver’s blood and urine samples tested positive for drugs (Cosbey, 1986). Benzodiazepines accounted for 87% of the positive results, diazepam occurring most frequently.

Heroin-dependent individuals have sometimes, but not always, been found to have poor driving records when compared with other groups. Babstet al. (1970) reported that 77% of heroin addicts had been involved in accidents (resulting in injury or death) compared with 20% of controls. None had been convicted of driving under the influence of drugs, however.
An explanation for this has been forthcoming and serves to illustrate the complexities of the possible relationships between drug usage and traffic safety. The specific purposes of the investigation on methadone maintenance patients reported by Blomberg & Preusser (1974) were to obtain data on the incidence of driving under the influence of narcotic drugs, on which the subjects had previously been dependent, as well as licit methadone, and to determine the incidence of narcotic drug use in traffic crashes and violations. A sophisticated matching procedure was carried out to obtain an opioid-free control population. Driving habits were examined (by interview and inspection of official records) for four periods; pre-drug, non-heroin, heroin and methadone. Of the respondents, 96% reported driving at least once during the heroin period and 94% during the methadone period (although only 74% and 66% respectively were licensed). The estimates of mileage driven exceeded the national average of 10,000 miles per year (even the unlicensed drivers drove more than 5,000 miles/year). “Personal” and “work-related” were the commonest reasons given for driving in the pre-drug and methadone periods but “to get drugs” was the commonest reason in the heroin period. Subjects who drove in the heroin period said that they often drove immediately after taking the drug. Examination of driver records revealed no differences between the methadone patients and controls in the distribution of all accidents or in those which caused injury or death. Compared with State-wide data, the accident rate per million miles driven was not significantly different during the methadone period and was lower in the heroin period (largely as a result of the great increase in miles driven). Violations data examination revealed a higher number of equipment offences during the methadone period but the number of more serious offences was not increased during the 5 years of the study. An overriding need of these
individuals (> 50% said this) to avoid detection of their heroin habit by coming to the attention of the police appeared to be a strong motivating factor during the heroin period, providing a powerful deterrent against unsafe driving behaviour. A similar pattern of results emerged from the study of Maddux et al. (1975).

Stevenson et al., (1986) identified a high-risk group of outpatients who had been involved in procedures which required sedation and analgesia. After treatment, they were required to return home either as a pedestrian or driver before they had regained "street fitness". It can be seen that the range of both prescription and illegal drugs user groups is broad and covers a large cross section of drivers. For example, complete recovery of the psychomotor performance of subjects from a single (75 mg) dose of pethidine did not occur until 7 hours after drug administration (Korttila & Linnoila, 1975).

The use of amphetamines and related drugs, particularly by drivers of long-distance heavy vehicles, presents a special case in that the drugs are used specifically to enhance driving performance, a manoeuvre which is not entirely successful. The use of stimulants to combat fatigue was widespread, especially by truck drivers. Over 40% of a New South Wales sample (n = 615) regularly used these drugs (Linklater, 1977; 1978). This problem would appear to have increased in Australia over the years since the Linklater studies (Smythe et al., 1991).

A series (n = 182) of heavy vehicle crashes in the U.S.A which resulted in the death of the driver was subjected to an in-depth examination (National Transportation Safety Board, 1990). One third of these drivers tested...
positive for alcohol and other drugs of abuse which included cannabis (13%), alcohol (13%), cocaine (9%), amphetamines (7%), other stimulants (8%), codeine (< 1%) and phencyclidine (< 1%). Stimulants were the most frequently identified drug class and their use represents a different expression of the drugs driving problem in that they were taken specifically to modify driving ability.

Although amphetamine-like drugs do alleviate fatigue, they also are well known to cause hallucinations (Cameron, 1973) and to increase aggression and risk-taking behaviour. Their effects are liable to wear off suddenly, leaving a reactive depression (Milner, 1972), and the drugs are subject to tolerance with repeated use which also has adverse cardiovascular consequences.

In the U.S.A., the barbiturates are among the most common prescribed drugs detected in drivers who are suspected of driving under the influence of alcohol or who are involved in an accident. Mason & McBay (1984) reported that in blood samples taken from drivers (n = 600) who were killed in North Carolina between 1978 to 1981, alcohol was found in 79.6% of cases, THC in 7.8%, methaqualone in 6.2% and barbiturates in 3%. Barbiturates, diazepam and other psychoactives were the most frequently found drugs by Lundberg et al. (1979) who examined body fluid samples from drivers who were apprehended in California on suspicion of drug-impairment. Ninety five percent of the samples were positive for drugs or alcohol.

The incidence of drugs other than alcohol in drivers who have been involved in traffic accidents has varied widely from location to location.
Cairns et al. (1984) examined 1,507 blood samples taken from road accident victims taken to the Waikato Hospital for treatment. Prescription drugs were found in only 2.7% of cases. The drugs found were anticonvulsants, diazepam, dextropropoxypheine, chlordiazepoxide, codeine, nitrazepam and thioridazine/orphenadrine. Only one sample was found to be positive for THC. A similar rate of detection for prescription drugs was found by Bailey (1987) who also examined road accident victims admitted to a New Zealand hospital (fatally injured persons were excluded). While alcohol was found in 20% of drivers, prescription drugs were found in only 2%. 6.5% of drivers had used cannabis during the last few days before the accident. A larger number of drivers admitted to using prescription drugs (8.3%) than was detected (2%) and this discrepancy may reflect poor detection methods.

In the United Kingdom, Everest et al. (1989) reported on the incidence of drugs in road accident fatalities (n = 1273). The overall incidence of drugs likely to affect the central nervous system was 7.4% and with the exception of diazepam (1.4%) and analgesics, no single medicinal drug was recorded at a rate which exceeded 0.5%. Drugs of abuse, notably cannabis at 1.6%, were proportionally most common among young and middle age male drivers and motor cycle riders, not infrequently associated with alcohol. A greater incidence of medicinal CNS active drugs was found to occur in road users of both sexes over 60 years of age.

Several studies have examined the blood of drivers who were killed in traffic accidents. Vine & Watson (1983) examined blood samples (n = 425) which had been taken for post-mortem alcohol determination. Alcohol was present in 51% and drugs were present in 10% of samples.
Alcohol combined with drugs were found in 6%. Illicit drugs were not tested for. Diazepam was found in 3% of the sample. Of the other drugs found were anticonvulsants, sedative hypnotics (barbiturates), and anti-inflammatory (phenylbutazone). Drugs known to impair driving-related skills were found in 37% of driver, rider and pedestrian fatalities (n = 191) in a study carried out in Victoria by Hendtlass (1985). Cannabis (20%) was detected most frequently followed by aspirin/paracetamol and then benzodiazepines.

McLean et al. (1985) examined blood samples taken from road accident victims (n = 48), those injured in road accidents (n = 37) and drivers who failed random breath testing (n = 115) and compared them with 387 controls taken from blood banks. Drugs and alcohol were found in 18.5% of cases from road users compared with 0.3% of blood donors. The prescription drugs found were CNS depressants (oxazepam, diazepam, amylobarbitone, phenobarbitone, diphenhydramine) analgesics, local anaesthetics and an anti-inflammatory. THC was found in 6% of samples.

Just because a drug is found in the blood of a dead or injured driver does not automatically mean that the drug played any part in crash-causation. However, in the Canadian study of Warren et al., (1981), after a rigorous exclusion procedure, 11% of cases remained where the presence of the drug could not be discounted as being contributory. Moreover, when the effect of alcohol was eliminated statistically, culpability was raised for tranquilisers, antidepressants, antihistamines and cannabis.

In summary, most of the analytical studies have found a 5-15% incidence of drug involvement in road crash victims, the variation appearing to
depend largely on whether cannabis was included in the screen (Cairns et al., 1984).

2. Evidence from a prospective study

There is one prospective study in the literature. Skegg, et al. (1979) followed a very large (n = 43,117) cohort of patients who were issued prescriptions over a period of two years and noted whether they were killed or injured in a road accident. There was a highly significant correlation between the prescription of minor tranquillisers and the risk of being involved in a serious crash. Those involved in the fatal accidents were 4.9 times more likely to have obtained a prescription for a minor tranquilliser than were the controls.

3. Evidence from behavioural studies

The World Health Organisation (Willette & Walsh, 1983) states that "there are important reasons for clearly understanding the relationship between drug concentrations in blood and other body fluids and impairment as a function of time after both acute and chronic dosing".

It is beyond the scope of this review to detail the drugs/performance literature. Many of the studies, especially those carried out before 1980, are methodologically and/or procedurally deficient and have proved to be of limited value in establishing profiles for the behavioural toxicology of drugs. Many are single-dose studies conducted over a limited time-course, and have usually examined only the pre/post drug paradigm. For example, Blum et al. (1964) allowed only short intervals of time between drug
ingestion and testing on various cognitive and psychomotor tasks, which resulted in non-significant results. These results possibly reflect the measurement of behaviour before the full effects of drug action had occurred.

Other studies have been conducted without placebo controls (Luscombe et al., 1983; Persson et al., 1980) or without pre-drug controls (Biehl, 1979; Luscombe et al., 1980). Greenblatt & Raskin (1986) in reviewing the use of benzodiazepines for psychotic disorders were highly critical of earlier uncontrolled studies and found that very few patients had been studied in well-controlled clinical trials with fixed-dose regimens. In fact, Barbee & Black (1985) have suggested that many studies using psychiatric patients as subjects had major flaws. Many of the patients were on other medications as well as the target drug. Other studies have used doses which were well below the therapeutic range and did not compare them with accepted therapeutic doses. For example, Melikian (1961) concluded that meprobamate (400 mg) did not impair subjects on any of the seven psychological tasks (mainly cognitive) used. The initial dose of meprobamate is usually 600 mg (Goodman & Gilman, 1975).

Thus, methodological improprieties, poor statistical analysis (Job, 1982) and failure to consider inter-individual variation in serum concentrations after standard doses (Sellers, 1975) have resulted in conflicting evidence concerning the various effects of both licit and illicit drugs on human performance. Questions such as the magnitude and time-course of drug effects remain largely unanswered.

Healthy volunteers, rather than patients, have been used as subjects in
most studies and while it can be argued that this is a logical place to start, such results take no account of a possible interaction between drug and disease state.

It is very important that attempts be made to characterise the relationship(s) which may exist between behavioural impairment and the pharmacokinetics of drugs. The questions of acute and chronic tolerance to drug effects and the interactive effects of drugs with alcohol should also be explored.

In a series of studies, the effects of three drugs, diazepam (a minor tranquilliser), pentobarbitone (a hypnotic or sleeping medication) and dexchlorpheniramine (an antihistamine) on driving-related performance have been comprehensively explored. The drugs have been given acutely and sub-chronically and the interactive effects of these drugs with "social" doses of alcohol have been investigated. In particular, attempts have been made to relate the observed decrements in performance to the blood levels of the drugs and of alcohol. As an example of the minimum amount of information which the authors believe should be available on the behavioural toxicity of a drug (as it affects human skills performance) which is used in medicine, and therefore likely to be taken by drivers, the effects of diazepam, alone and in combination with alcohol, will now be discussed (Starmer et al., 1992 a,b).

With acute doses (5, 10, 20 mg) of diazepam (Starmer et al., 1992 a), plasma diazepam concentrations were significantly increased when alcohol (0.75 g/kg) was given concomitantly because of a decrease in the rate of conversion of diazepam to the less active metabolite, nordiazepam (N-
desmethyldiazepam). There was also a delay in the time at which the peak plasma diazepam concentration was attained in the alcohol-treated groups, indicating an absorptive interaction. Although alcohol had a marked effect on the pharmacokinetics of diazepam, diazepam appeared to be without effect on alcohol kinetics and the rate of elimination of alcohol was unaffected by diazepam pre-treatment.

When alcohol was given after diazepam, impairment continued for a longer period than when the same dose of diazepam was given alone. This can be considered, in part, to be due to a combination effect which might be expected from two drugs with similar modes of action, but there were also absorptive and a pharmacokinetic interactions which resulted in raised diazepam concentrations. The pharmacokinetic component is thus an important factor in any explanation of the interactive effects of alcohol and diazepam on human skills performance (Aranko et al., 1985a,b).

An attempt was made to explore the relationship between impairment and the plasma diazepam and alcohol concentrations. The mean impairment and diazepam concentration curves were shown to have similar profiles over time. Although very few significant correlations between impairment and diazepam plasma concentration were found for subjects given diazepam alone, the number of significant correlations was greatly increased in those who received diazepam and alcohol.

Peak impairment of performance and peak plasma diazepam concentrations were coincident for many subjects. For all subjects and all test parameters (digit symbol coding, tracking control, standing steadiness), the maximum separation was 20 minutes. Other studies have reported similar results
Individual and group hysteresis curves were plotted to characterise any tolerance effects which might have occurred. A hysteresis curve is a time flow plot, with drug concentration on the X-axis and performance score on the Y-axis. Many of the individual hysteresis plots indicated the development of acute tolerance to diazepam. At similar plasma diazepam concentrations, impairment was found to be greater on the onset phase when compared with the offset phase of the hysteresis curve. Some individual hysteresis plots also displayed a second impairment peak which might relate to an accumulation of the active metabolite of diazepam, N-desmethyldiazepam.

An onset/offset phase analysis was also carried out on the results which were separated according to whether they fell on the rising side or on the falling side of the plasma concentration curve. When such an analysis was conducted on the individual pooled data for subjects given diazepam alone, no relationship between diazepam plasma concentration and any of the pharmacodynamic parameters was found. Hommer et al., (1986) have reported similar findings. Poor correlation between performance on similar tests (digit symbol coding, standing steadiness) and concentrations of total diazepam, N-desmethyldiazepam and free diazepam has also been reported by Swift et al. (1985).

In subjects given alcohol and diazepam, significant linear relationships between diazepam plasma concentration and performance decrements were found.
Most reports in the literature have stated that the concomitant administration of diazepam and alcohol result in decrements in performance which are mainly additive when compared to the effect of diazepam alone (Morland et al., 1974; MacLeod et al., 1977; Mattila, 1984). With the tests used in this study, the performance decrements were invariably greater after the combinations of alcohol and diazepam than when the same doses of diazepam were given alone and the interactions were again suggestive of additivity.

Given that diazepam has sedative activity, it is interesting to note that although subjects reported a strong sense of sedation and a loss of co-ordination when given diazepam, either alone or in combination with alcohol, the differences from pre-drug scores were not significant. This may have been due to the small number of subjects tested and/or the increase in sedation and reduced co-ordination reported by the placebo group. The experience of the placebo group probably reflects the demands of the experiment. Subjects in all groups, reported an unwillingness to drive in their 'present condition'.

Strong evidence for 'rebound impairment' was given in the subjects' self-reportage. Although subjective indicators of impairment suggested that they had returned to pre-drug levels of competence by the end of the experiment (after 6 h), many reported impairment later in the day. This was often described as 'substantial exhaustion' and resulted in deep sleep for 12 or more hours. Clearly this has important implications for drivers and requires further investigation.

It has long been recognised that investigations into the chronic effects of
Benzodiazepines are made more difficult by an interplay between the effects of cumulation and tolerance. The sedative effects of diazepam have been found to decline over the first few weeks of chronic administration, despite cumulation of diazepam and N-desmethyldiazepam.

It was thus considered important that the nature and extent of any impairment which might occur when diazepam (5 mg, three times a day) was given for 8 days be investigated (Starmer et al., 1992b). Plasma diazepam and nordiazepam concentrations were monitored and comparisons were made between performance on the first and last day of treatment. The interactive effects of challenge doses of diazepam (10 mg) and alcohol (0.75g/kg) were also investigated.

Cumulation of both diazepam and N-desmethyldiazepam was evident by day 8. It has been reported that although cumulation of diazepam and N-desmethyldiazepam occurs during the first week of chronic therapy, a steady state between cumulation and elimination is achieved at some time during the second week (Hillestad et al., 1974). In this study, when alcohol was added to the diazepam challenge, the metabolism of diazepam to N-desmethyldiazepam was delayed. This was more apparent on day 8 than on day 1 and is similar to the findings in the acute study.

Despite the cumulation of diazepam by day 8, no significant impairment was found on the performance tasks prior to the challenge dose of diazepam. An improvement in performance from the baseline score on day 1 was found for most of the treatment groups in some tasks but was not significantly different in others. The performance of those who received a diazepam; plus alcohol challenge was significantly impaired on both day 1
and day 8. Although the group which received a diazepam challenge had longer reaction times on both day 1 and day 8, the differences from pre-drug performance were not significant.

Failure to detect significant impairment after diazepam alone on day 8 might be explicable in terms of the high inter-subject variability in plasma diazepam concentrations. The diazepam levels found 20 minutes prior to the challenge dose of diazepam ranged from 222ng/ml to 690 ng/ml. A similar variability was evident 90 minutes after the diazepam challenge dose.

Impairment could not be correlated with the plasma diazepam concentration. For example, the performance of one subject with a pre-challenge diazepam level of 222ng/ml was impaired after diazepam, even though his diazepam concentration did not increase substantially after the diazepam challenge dose. Another subject with a pre-treatment diazepam level of 575 ng/ml showed no impairment although his post-treatment level rose to 765 ng/ml.

A significant reduction in co-ordination was reported by the groups which received diazepam plus alcohol and alcohol alone on both day 1 and day 8. Although those challenged with diazepam alone reported a reduction in co-ordination and increased sedation on day 1, there was evidence for tolerance to the loss of co-ordination and sedative effects by day 8. When the sleep patterns of the subjects taking diazepam were compared with those of the placebo group, some differences were found. The diazepam treatment group reported a faster sleep onset, fewer night-time awakenings and a longer night-time sleep, but they also reported feeling less rested on
awakening in the morning.

The results of this study suggest that the development of behavioural tolerance to diazepam may not be achieved after one week of chronic usage and that users of this drug may need several weeks to overcome impairment.

The importance of behavioural toxicological testing in the laboratory stems from the fact that it is obviously unrealistic, in the first instance, to examine for drug-related impairment of driving performance in real-life traffic situations. Laboratory tests which will detect the potential of a drug to impair driving ability are available but must be shown to be both sensitive to the effects of the drug and to be relevant to driving performance (construct validity). Construct validity is the degree to which a test captures the hypothetical quality or trait which it was designed to measure. Tests which are use to demonstrate drug effects which are relevant to driving should provide dependent variable which are simultaneously valid in two dimensions. They should accurately measure some specified pharmacodynamic effect, which is likely to impair driving performance, and also some mental function which is considered to be essential for safe driving. Painstaking work of this nature appears to be the only way to accurately assess the potential of drugs to impair driving performance and thus increase crash-risk.

There is a need for the international co-ordination of such research which will prevent unnecessary duplication and help in setting research priorities. Wolschrijn et al.,(1991) have established a new categorisation system for drugs affecting psychomotor performance by distributing a questionnaire,
worldwide, to 45 psychopharmacologists who were asked to classify drugs into those which were unlikely to produce impairment, those which might produce minor to moderate impairment and those which were likely to produce severe impairment and those which were likely to produce severe impairment and should, therefore be considered to be dangerous. This "Netherlands System" is a major advance in helping to understand which drugs may impair driving. It is an important guide for physicians and pharmacists and can be used to order research priorities but, because it uses drug dose and not drug concentration, it may not be useful to policy makers concerned with reducing the incidence of drug related crashes.
Conclusions

1. Given the epidemiological and behavioural toxicological evidence, together with a very limited amount of evidence from prospective studies, it appears reasonable to conclude that some drugs have the potential for impairing human psychomotor skills which are relevant to driving. There are also some fragmented pieces of evidence to suggest that drug-induced impairment of driver performance constitutes a traffic safety problem.

2. For a variety of reasons, most of which relate to dose and pharmacokinetics, alcohol is not a suitable model for the study of the effects of a drug on driver behaviour. Apart from these reasons there is the prospect that a driver may be safer with his medication than without it and this has ramifications to the complex interactions between medical conditions and drug treatments as they affect driver behaviour.

3. Possible countermeasures might include a requirement by the drug regulatory agencies for the generation of information on the behavioural toxicology (adverse effects on human skills performance) of new drugs before marketing. This should include, at the very least, an indication of the effects of the drug across the projected therapeutic dose range, both alone and when combined with "social" amounts of alcohol. The extent of the information which needs to be available has been explored in this review for one drug, the tranquilliser, diazepam. Information gathered in this way should be disseminated to health professional and the general public so that the appropriate choice of medication could be
encouraged and information/warnings made available.

4. The laws for driving under the influence of drugs are considered by some to be inadequate (largely because they are based on the alcohol model). It is to be hoped that new epidemiological findings, together with more objective methods of assessing driver intoxication, may provide a more rational basis for the control of drug-impaired driving. This is especially important where driving has been affected by the use of illicit euphoriants or by the recreational use of prescription drugs.

5. In the long term, however, the development of less-impairing prescription drugs by the Pharmaceutical Industry and the enthusiastic marketing of these is most likely to improve the situation. There are signs that this process has begun to occur with the new antihistamines (e.g. terfenadine, loratidine and astemizole), a tranquilliser (buspirone) and two antidepressants (fluoxetine and paroxetine) for example which are considerably less sedating than their older counterparts.

6. An important priority is to establish the extent and nature of drug use and abuse among drivers. Then the findings for drugs in compromised populations of drivers can be put into context and the design of any new studies which might be envisaged can be optimised. This is the objective of the current Federal Office of Road Safety Research Programme on Drugs and Driving.
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