Older drivers, illness and medication

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Older drivers, illness and medication

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Although this report was commissioned by the Department, the findings and recommendations are those of the authors and do not necessarily represent the views of the DfT.

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Executive Summary

This document has considered in detail the separate and combined effects that being old, ill and taking medication may have on the safety of older drivers and their risk level. The main points are summarised below.

1. This is a sector of the driving population that is not only growing in number, but is changing in make-up and behaviour. The biggest increase in active licence holders is older women. *A medical practitioner can now rarely assume that any adult patient is not a driver*. For example, in 1999, 64% of men aged over 70 and 22% of women aged over 70 were full car licence holders, but projections suggest that by the years 2020 to 2025, 78% of men and 58% of women over 70 will be licence holders (Maycock, 2000). This indicates an increase not only in proportion, but also in number, since the population in the older age group is increasing, as is the distance travelled by older people, particularly by older women. Despite this, there has not been a corresponding increase in serious accidents to older drivers. Any such increase in accidents is only apparent for the older old female drivers, and this is far less than the increase in mileage or numbers of licensed drivers in this age group. Their serious casualty involvement as drivers continues to be very low as a percentage of all serious casualties.

2. An older person's risk of being killed or suffering a serious injury as a result of any road accident is between 2 and 5 times greater than that for a younger person because of their increased frailty. The important thing to be aware of when considering any statistics that seem to state that older people have more accidents than middle-aged people is that most of these statistics are based on number of drivers killed or seriously injured. When statistics based on all severities are examined, there is no age-related increase in number of accidents for the over 60s. Mitchell's (2000) fragility index demonstrates that a given accident is three times more likely to be fatal for a driver, passenger or pedestrian aged 80 and over than it is for an accident victim aged 60.

3. General practitioners and other prescribers are not always aware of whether their patients drive or not, and may assume, erroneously, perhaps because of their age or gender, that they do not. Statistics on the increased and increasing proportions of older people who drive, particularly of older women, suggest that such assumptions are increasingly likely to be inaccurate. Studies have suggested that it is not uncommon for older drivers to be taking medication with which driving is contraindicated and for GPs to be unaware of whether their patients drive or not. Improved record keeping and more frequent medication reviews, especially where repeat prescriptions are used, are recommended by these studies, but the role of the patient in taking an active role in ensuring their doctor is aware of all the medication they are taking, (including OTCs), initiating reviews and asking questions about their medication must also be emphasised.

4. Older people commonly experience changes in motor, sensory and cognitive abilities, and are less sensitive to changes in their own performance than middle-aged people. These changes are usually small, but highly interactive: a combination of several such limiters can result in marked changes in efficiency. The reserve with which people compensate for reductions in various capacities is reduced, and older people are slower to recover from

lapses. Importantly, reserve cognitive capacity may be limited, leaving reduced ability to compensate for further deficits brought about by illness or medication. Reduced cognitive function may mean that self-awareness of changes in performance brought about by illnesses or medication may not be accurate. This suggests, for example that the 'if affected, do not drive…' clause in prescription labelling may need review in the case of older patients.

5. Doctors' underlying knowledge of matters concerning fitness to drive may need updating and emphasising more in training. Studies have shown that doctors' knowledge of the driving restrictions for specific illnesses is often poor, and that many doctors are not aware of the current age for licence review for fitness to drive. In studies, few knew where to get this information if they needed it. However, most knew that the responsibility for informing the DVLA of certain illnesses lies with the driver themselves, but that in certain circumstances it is legitimate for them to breach patient confidentiality and inform the DVLA if a patient continues to drive contrary to advice, presenting a threat to the public. The role of the doctor in most circumstances is to advise the patient that their condition presents a risk and requires notification. Evidence suggests that most older people are well-motivated to reduce such risk. However, many older people could be helped to maintain safe driving, rather than simply give up, if they were given specific advice appropriate to their condition, for example, to reduce driving in poor light, or seek vehicle adaptations. It is generally agreed that older people are at more risk as pedestrians than they are as drivers (Mitchell, 2000).

6. It is important to remember that each medication or illness is only one contributor to the pattern of influences that affect a person's safety as a driver. A 'severity of all combined effects' model needs to be considered for each patient. First and foremost, the patient is being prescribed a medication because they are unwell and in some cases the medication may improve their safety. The vital point is not whether the specific drug or illness may have an effect on driving performance, but rather, whether the individual is capable of functioning safely in their environment. A particular drug that may have a small effect on reaction time, may be the factor that tips the balance between driving safely or not for someone who has other deficits, but may be adequately compensated for in another person who otherwise has few difficulties. In considering whether to advise restricting or suspending driving or making prescribing decisions, the end functional capacity, rather than individual sources of functional loss is the main concern. That is, one needs to take into account the severity of impact of all combined effects, and importantly, one needs to consider how much compensatory potential the older driver may have to compensate for a particular deficit.

Making a judgment based on one drug, or on a specific diagnosis without considering other factors is never appropriate, but is even less relevant for older people in whom comorbidity and normal age-related deficits are common, in addition to the frequency of polypharmacy in this group.

It is suggested that doctors and other professionals in advisory capacities consider whether each of the following factors are present and to what extent they may be affecting driving or general cognition: difficulty with movement or motor control, impaired visual abilities, impaired cognitive factors, diagnosis and severity of illness, type of drug therapy. It is

suggested that a serious difficulty or possible effect on driving in any one area may mean that driving is too risky, at least for the time being. More commonly, minor effects in more than one of these areas will combine to reduce the driver's 'reserve capacity' for coping with demanding or unexpected driving situations, and may also mean that driving is too risky, at least for the duration of a prescription or illness, or that further detailed assessment is needed.

7. The better-known accident statistics linking medical factors and driving accidents are based on the most extreme scenario, that of becoming unconscious at the wheel. This being a very rare occurrence, has resulted in a worrying belief that medical factors are contributing very little to the safety of drivers. Evidence from a wide variety of studies has been considered, but studies which separate out at fault from not at fault accident victims, and which control for age either statistically or by use of non-accident involved or not at fault age matched controls, are particularly informative, since they give opportunity for examination of medical factors that are in addition to general age-related changes in function (e.g., visual function). Studies of actual accident data have been emphasised where available. Difficulties in generalising results of simulator, test track and neuropsychological testing to actual driving in traffic are acknowledged, but it is also recognised that in some situations, these methodologies are extremely useful predictors of aspects of driving, and that in some circumstances ethical considerations mean that on-road driving would be inadvisable.

8. Some illnesses are specifically associated with higher road accident risk.

Bearing the above points in mind, the following is a list of illnesses shown to be associated with increased crashes; epilepsy, diabetes, heart disease, excessive sleepiness, particularly that associated with narcolepsy and obstructive sleep apnoea, dementia (various types), psychiatric illness, specifically anxiety, depression, alcoholism and behavioural/personality disorders. In addition to the cognitive effects of the illness and the medications, depressed people have also been known to commit suicide by causing a vehicle accident. Many of these illnesses increase in frequency with increasing age, and effects, for example, on cognition, add to already existing age-related deficits.

Although having a stroke at the wheel is clearly associated with accidents, a diagnosis of having had a stroke is not reliably related to increase in accidents in those who resume driving. Many stroke patients do not resume driving, and many resume driving with self-imposed restrictions, such as avoiding motorways or busy times. Although examinations of driving in stroke patients has revealed that they have many difficulties, the important points to make are that many patients can be helped to resume driving safely with training and perhaps vehicle adaptations, and actual functional capability of the individual is the key issue in giving advice; knowledge of which often requires referral for detailed testing.

The case of dementia deserves special comment here. It is important to note that not all studies find an increase in accident risk amongst those with a diagnosis of dementia who are still driving. The two significant reasons for this are (i) Patients in the early stages of their disease may not yet have impairments that seriously affect their driving, again, actual function, rather than diagnosis is the important issue. Early stage or mildly affected patients often form the bulk of dementia patients in such studies (ii) Some patients, even those with

more serious impairments, are greatly reducing or restricting their driving, either on their own initiative or under advice from medical practitioners or friends and family, significantly reducing their risk. Most patients with more severe impairments do give up driving and it is generally agreed that these patients would present serious risk to themselves and the public as drivers if they were to continue.

Some illnesses that may appear to be extremely likely to increase risk of accidents are not shown by studies to do so. Parkinson's disease is one such example, with the simple reason that patients with severe functional impairments find themselves unable to drive and so give up. The result is that populations studied rarely include severely impaired patients. Another example is syncope, in which patients who have poor warning of a fainting attack generally recognise that this condition is too risky for driving and so suspend driving until their attacks cease. Patients in any study are therefore likely to be those in whom the pre-syncope warnings are clear and of sufficient duration to pull off the road.

9. There is reliable evidence that certain prescribed drugs do increase the risk of road traffic accident, especially for older drivers. For example, anxiolytics as a class produce up to 5-fold increase in risk. These measurements would be greater in an older driver population due to the changes in metabolism of such drugs and the added factor of other existing limitations in driving ability. Studies indicate that between 6 and 13% of accident-involved drivers have taken medications with probable Central Nervous System (CNS) effects (the frequency of these medicines in the general population is 2-5%). A higher incidence of the prescription of psychoactive drugs has been demonstrated in over 60s who have been killed in road traffic accidents compared with other age groups, and this increases dramatically for older men in particular, from 6.6% of fatally injured men aged 65 to 74 years to 23.3% in those aged over 75.

10. Some drugs are specifically associated with higher road accident risk, and some of these have greater effects on older people than on younger people.

A central issue in this document is that older people can react differently to many drugs than younger people.

Changes in lean body mass, body water, proportion of body fat and in excretion, homeostatic mechanisms and receptor sensitivity all lead to differences in the plasma or tissue concentration, how long a drug's effect lasts, and level of a drug necessary to have an impact. The net effect is that older adults exposed to many classes of drug will have higher active levels of the drug for a longer time. Also CNS effects tend to increase with age due to the neuronal loss and decrease in cognitive reserve as a result of the normal ageing process.

11. Although the details of the effects of different drugs is a vast area, the main point to make in this summary is that in many cases a suitable alternative medication may be available that presents a lesser risk to driving. In addition, assumptions that major driving impairments will only occur early in the course of treatment, and that tolerance will develop, are unsafe; studies demonstrate variability in the tolerance development between different neuropsychological attributes, while others suggest, for example, that the risk associated with long half-life benzodiazepines does not decrease significantly with continued use.

Particular classes of drugs and of side effects are related to significant difficulties specifically for driving and in older people. Key examples are cited below:

Drugs with anticholinergic effects

These have been shown to be associated with significant visual and neuropsychological impairments, including attention deficits and reduced ability to process information. Older patients are known to be more sensitive to the impairing effects of anticholinergic medication, although specific studies relating such effects to driving risk in older people have not been found. This may be an important field for future research. Many classes of CNS medication have anticholinergic side effects, the most notable being found among the older antidepressants and among antipsychotics.

Antihistamines

Older people have been shown to be more sensitive to the sedating and anticholinergic effects of both antihistamines (H_1 antagonists). Many of these drugs have been related to significant impairments in actual driving, with some showing greater impairment in female drivers than in male drivers, effects being reported for non-sedating, second generation antihistamines as well as in the first generation sedative antihistamines. That is, although second generation antihistamines should be chosen for drivers, it should not be assumed that they are risk-free. Studies have shown that self-assessment of perceived drowsiness is poorly related to level of driving-related impairment, and therefore self-perception of whether or not one is affected by the sedating properties of such medications should not be relied upon in decisions of whether to drive or not.

H_2 antagonists have been shown to impair the metabolism of alcohol, resulting in higher blood alcohol concentration (BAC) than expected. Combined with the effects of increasing age on alcohol metabolism, this may produce an increased risk of accidents on the road for older drivers.

Benzodiazepines

These drugs have been associated with acute confusional states and chronic cognitive impairment in older adults, and changes in pharmacokinetics in older patients may mean that effects of these drugs may be cumulative. Studies with benzodiazepines have found significant impairment in cognitive and psychomotor functions related to driving, in risk taking behaviour, and in actual driving. Significant increases in accident rate have been related to this class of drugs in epidemiological studies, both in the general population and specifically in older populations, although an age effect in this increased risk has not been found – older people taking this class of drugs have not been shown to be at greater risk of an accident than younger people taking the same drugs. There is evidence that both anxiety, for which benzodiazepines are commonly prescribed, and the medication itself cause an increase in accident rate. However, careful studies suggest that these effects may be independent of each other.

Hypnotics

The purpose of these drugs is to induce sleep. Insomnia is a difficulty that increases with increasing age. The issue for drivers is whether they have significant impairing effects on driving the next day after a hypnotic has been taken the night before. Greater risk of road accidents has been found with those drugs that take longer to be eliminated from the body (long half-life) than with shorter half-life drugs, both with younger and older patients. However, the short acting hypnotics are not without risk, extent of increased risk not being reliably related to half-life. Zopiclone is one medication in this class of drugs that has a short half-life but which stood out in one important study as being related to an increase in risk of accident.

Antidepressants

This is a class of drugs where there is a particular problem for the researchers in disentangling the effects of the medications and of the illness itself, depression causing significant cognitive and motor slowing that affects driving. Antidepressants are divided into several sub-classes, the older tricyclic antidepressants (TCAs) having more significant effects on driving related abilities, particularly in older patients, than the newer drugs such as selective serotonin reuptake inhibitors (SSRIs) and other such specifically acting drugs. An important point to emphasise is that, although traditionally it is thought that cognitive impairments due to the drugs are counteracted by improved cognition once the therapeutic action of the drugs is developed (several weeks after onset of treatment), studies do not confirm this. One study examining accident risk in older drivers found a tendency for risk to increase with duration of use of TCAs beyond 30 days, and other studies have indicated that increased risk is significant only for the older drivers in the study. Several sources now recommend avoidance of TCAs for the elderly.

Opiates and Opioids

These drugs are frequently prescribed for older patients and may be present in OTC medications for pain and diarrhoea. Sedation and drowsiness are important side effects of such compounds. However, although studies specifically examining their effects in older drivers are rare, one such study did find an increased crash risk for older drivers using opiate analgesics (Leveille et al., 1994). In contrast, other studies have found a reduction of risk, and have attributed this to reduction of severe pain.

Non-steroidal anti-inflammatory drugs (NSAIDs)

These drugs have been associated with increase in accident risk in several studies, and have also been associated with specific memory and concentration disturbances in older patients. Importantly, the effects of these drugs may be independent from the effects of the illnesses for which they are prescribed (commonly arthritic symptoms).

Finally, polypharmacy is more common in older people and the consequences of such combination of medication needs to be considered. In general, alcohol is a serious exacerbator of risk in older people.

1 Summary

Changes in the make-up of our population and society in general mean that more older people are driving and continuing to drive, and older people are driving many more miles than ever before; it can rarely be assumed that any adult patient does not drive.

However, older people are more likely to be suffering from serious illnesses, often from several different disease processes, and are more likely to be taking prescribed medication that may influence their ability to drive safely. This is in addition to any age-related cognitive and physical limitations they may be experiencing. Older people are also much more vulnerable to injury and death in an accident because of their increased physical frailty.

In addition to the added complication of normal age-related changes which may affect driving skill, and the increased incidence of disease, older patients are a particular concern with respect to the effects of medication because of changes in metabolism and reductions in spare capacity in both physiological terms such as homeostatic mechanisms or efficiency of drug excretion, and in cognitive terms such as reduced information processing capacity, reduced peripheral attention and speed of reaction. It is suggested that a model of 'severity of all combined effects' is the most appropriate one to take when giving advice to older patients, taking into account any obvious evidence of normal age-related changes, such as changes in eyesight, speed and strength of movement, slowing of reaction times, in combination with the possible effects of disease and the medication prescribed.

This document presents all of these these points in greater detail, giving a summary of studies involving illnesses commonly associated with age and of commonly prescribed medication of particular concern in relation to driving performance and risk.

2 Introduction

This document sets out to provide physicians with enhanced information as to the driving related effects of illness and prescribed drugs specifically for older people. It is not intended to replace other sources of drug information, or to be an exhaustive account of all drugs available. Instead, commonly prescribed drugs with potential and observed effects on driving performance are indicated, with special reference to the specific effects such medication may have on an older person. The important point to bear in mind when making decisions as to the most appropriate therapy in relation to driving is to what extent the possible effects of a particular drug on driving-related abilities can be considered, given the health needs of the patient. However, in many of the driving-related studies reviewed we do not know whether the medicine being taken is the cause of any increased risk, or the illness that results in the medicine being necessary, the medicine itself possibly reducing the risk of the ill person. An area that exemplifies this difficulty is in treating chronic insomnia where both the problem and the treatment can result in daytime drowsiness. Where possible, studies that attempt to separate out such effects are considered.

In common with other sources in the literature, 'older' is defined as over 60, and this is further divided in some circumstances into 'younger old' and 'older old' with a general cut-off being taken as 70 years. Where data specifices particular age ranges that are different to this, details are given. Nevertheless, it must be emphasised that the most salient finding in the gerontological literature is the increase in variability of function with age, with some older people showing little change in function from their youthful levels, and others showing serious impairment.

There are several vitally important factors for the physician to bear in mind when prescribing for older patients:

2.1 Increase in numbers of older drivers and amount of driving done

More older people are active drivers than ever before. The biggest increase in recent history in active licence holders is older women. One can now rarely assume that any adult patient is not a driver. For example, there was a 200% increase in male drivers over 65 and a 600% increase in female drivers over 65 between 1965 and 1985 as compared with a 29% and 290% increase in drivers (male and female) aged 17-59. The figures in Table 1 opposite illustrate that in 1997/99, the National Travel Survey (2000) reported that the number of men (all ages) holding full driving licences was about 11% higher in 1997/99 as compared with 1985/86, but the number of women holding full driving licences was about 44% higher. The difference between numbers of older men and women drivers is diminishing rapidly. This was demonstrated by a generally advertised survey in 1995-96; Rabbitt, Carmichael, Jones and Holland (1996) received 55% men and 45% women driver respondents over the age of 54. According to the 1992/94 population census, 48% of all people in the UK aged over 60 lived in households with at least one car. Table 1 opposite summarises the UK statistics for the over fifties from 1975 to 1999. Table 1 also includes projected figures,

from Maycock (2000). Maycock (2000) projected proportions of older people licensed to drive in the year 2022, using population trends (e.g., findings of greatest increases in numbers of younger old, particularly numbers of men aged 60-74), and trends in life expectancy (e.g., trends for the difference in life expectancy between men and women to continue to even out, men showing greater gains in life expectancy than women, who traditionally have longer life expectancy). His projected figures are shown as percentages, with projected numbers these figures represent, based on population projections, in brackets.

| Years | 1975/76 | | 1985/89 | | 1995/97 | | 1997/99 | | 2020/25 | |
Age group	M	F	M	F	M	F	M	F	M	F
60-69	59	15	72	24	83	46	84 (2,169)	51 (1,325)	94 (3,407)	86 (3,174)
70 plus	33	4	51	11	65	22	64 (1,597)	22 (752)	78 (3,043)	58 (2,805)
All adults	48		57		68		70			

Table 1: **Percentage of the population who were full car driving licence holders in the years 1975 to 1999, by age and sex, with *projected* data for the years 2020/25. Absolute numbers (000s) are given in brackets for 1997/99 and for projected data**

Source: Transport statistics Bulletin: National Travel Survey: 1997/99 update, Government Statistical Service and Maycock, 2000).

These figures indicate that as the number of older people in the population increase, the absolute number of older drivers is expected to increase. In addition, the proportion of older people who are drivers is also increasing. The differences between the proportion of men and women who are drivers is reducing as more women of all ages are now drivers and expect to continue to drive as they get older. UK Population Trends (2000) reports that the biggest increase in recent years in population has been for the older old population – for example, there was a 27% increase in numbers of people over the age of 85 between 1991 and 1999.

In addition to increases in the number of older people who are drivers, the amount travelled by older people is also increasing. For example, Transport Statistics: Focus on Personal Travel (DLTR, 2001) compared with data from Focus on Personal Travel 1985/86 illustrates that women aged 60-69 increased their average annual distance driven by over 187% between 1985/86 and 1998/2000 (men by 52%) and older old women aged over 70 by 243% (men by 95%).

Despite these increases in numbers of licensed older drivers, and also increases in mileage of older drivers in recent years, there has not been a corresponding increase in serious accidents to older drivers. The percentage changes are illustrated in Table 2.

Table 2:	**Number of car drivers killed or seriously injured for drivers aged over 60: 1981-85 and 1994-98 averages, and 2000 figures. From Road Accidents Great Britain, 2000 and 1999 reports (DLTR)**			
	1981-85 average	**1994-98 average**	**2000**	**% change since 1981-85**
Men				
60-69	908	613	569	-37%
70+	641	708	642	+<0.01%
Women				
60-69	299	299	264	-12%
70+	221	323	308	+39%

This table illustrates that any increase in accidents is only apparent for the older old female drivers, and this is far less than the increase in mileage or numbers of licensed drivers in this age group (see figures above). The serious casualty involvement of women over 70 as drivers continues to be very low as a percentage of all serious casualties at 1.7% for those aged 60-69 in 1981-85 increasing to 2.1% in 2000, with similarly small increases for older old women drivers (70-79: 1.0% in 1981-85, 1.7 in 1999; 80+: 0.2% in 1981-85, 0.7% in 2000 of total road accident casualties). Such statistics demonstrate that older drivers (over 60) make up a smaller proportion of seriously injured or killed drivers (14% total) than would be expected from the population (over 60s make up approximately 20% of the UK population).

2.2 Risk of being killed or seriously injured as a driver

The often quoted statistics demonstrating that older people have more accidents as drivers than those in the safest group, the 30-59 year olds, are based on numbers of drivers killed or seriously injured. When statistics based on all severities are examined, there is no age-related increase in total number of accidents for the over 60s (Road Accidents Great Britain, 2000). There are, of course, no statistics anywhere claiming that older people have anything like the number of accidents that younger drivers have. For example, in 2000, 4,777 drivers aged under 30 were killed or seriously injured on British roads, but only 1,783 people aged over 60 were killed or seriously injured, and the rate per 100,000 population of *all severities* accidents as drivers for the 60-69 age group was 128, whereas for the 20-29 age group it was 515. However, an older person's risk of being killed or suffering a serious injury as a result of any road accident is several times greater than that of a younger person because of their increased physical frailty. That is, although older people may not be having a greatly increased number of accidents, they are at higher risk of serious injury or of dying as a result of any accident they are involved in. This is clearly illustrated by Mitchell (2000), who calculated a fragility index by normalising the percentage of accidents that are fatal to be 1.0 for the age group 20-50. He found an increasing fragility index for car drivers, passengers and pedestrians of 1.75 at age 60, 2.6 at age 70 and 5.9 for people aged 80 and over.

2.3 Studies of the influences of medical factors on driving

The better-known accident statistics on the link between medical factors and driving accidents are based on the most extreme scenario, that of becoming unconscious at the wheel. This, being a very rare occurrence, has resulted in a worrying belief that medical factors are contributing very little to the safety of drivers. For example, in a document widely available to General Practitioners (GPs), Taylor (1995, Medical Aspects of Fitness to Drive. The Medical Commission on Accident Prevention) states that only 1 hospital admission accident in 250 has an associated medical factor, but the table of 'medical factor accidents' provided is actually a table of causes of road accidents involving collapse at the wheel. In contrast, studies of the existing medical conditions of drivers who have been involved in road accidents are perhaps less well known among GPs, but are perhaps more indicative of the wider influences of medical factors in driving. In particular, studies which separate out at fault from not at fault accident victims, and which control for age either statistically or by use of non-accident involved or not at fault age matched controls, are particularly informative, since they give opportunity for examination of medical factors that are in addition to general age-related changes in function (e.g., visual function). Studies such as this are considered throughout this document, but to illustrate, one such study by Rehm and Ross (1995) found that 79% of at fault older drivers had significant underlying medical problems, as compared with 52% of not at fault older drivers.

2.4 Importance of General Practitioners' data regarding older patients

General Practitioners' information about older patients is often incomplete. A study by Cartwright (1990) found that GPs were often unaware that their elderly patients lived alone, drove or drank alcohol, even when they were taking prescribed medications for which drinking and/or driving were contraindicated. Just over a third of older people in this study were taking prescribed medicines of which their GPs were apparently unaware (a finding also reported elsewhere – Cartwright cites Price, Cooke, Singleton & Feely, 1986). Of the hypnotics, sedatives and anxiolytics, 36% were assessed as having been prescribed in too large a dose for the patient. Seven per cent of the medicines taken for which driving was contraindicated were taken by patients known to drive by their GPs, and a further 40% by patients whose driving status was not known to their GP Although many GPs now have improved computerised record facilities, this is an issue of which all GPs need to be aware. The ongoing study of older drivers conducted at the Age and Cognitive Performance Research Centre in Manchester has found that 6% of respondents were taking traffic dangerous drugs, mainly hypnotics or antidepressants, in some cases in quite high doses, suggesting that their GPs were perhaps not aware that they drove, or that the patients were ignoring instructions not to drive while on this medication. Cartwright recommends better records, regular supervision and more frequent review of medicines, especially where repeat prescriptions are used. However, he also emphasised the role of the patient as a member of his or her primary care team in ensuring that their doctor is aware of all their medicines, side effects and medical problems, and also in initiating a review of medications by asking questions such as 'is this new prescription in addition to or instead of the existing drug?'

and making appointments periodically to check if they should still be taking repeat prescriptions. Finally, Cartwright recommended that clinical audit should check that information on patients' alcohol use and on their driving is available when medicines for which these are contraindications are prescribed.

2.5 Roles of the driver and of the Medical Practitioner

In the UK, the main responsibility for deciding whether a patient is fit to drive or not rests with the driver themselves and ultimately the DVLA, rather than with the doctor, although the doctor's role in advising is crucial. The Road Traffic Act (1988) states that a driver must inform the Driver Vehicle Licensing Authority (DVLA) and their insurer themselves if they have a relevant condition or disability, upon being made aware of this condition. However, it is the doctor's responsibility to inform patients that they have a condition that requires them to stop driving, and to give advice. Some studies have shown that doctors' knowledge of DVLA recommendations for particular conditions is not always thorough. Kelly, Warke and Steele (1999) conducted a face-to-face interview study, asking basic information of 50 doctors who all came into contact with older patients regularly (GPs, Geriatricians). The participating doctors did not have chance to prepare, the interview being conducted in a naturalistic manner in their places of work. Less than half knew that the correct age for licence review for fitness to drive was 70 years old, and only 9 knew that the subsequent frequency of licence review was every 3 years. Doctors' knowledge of medical conditions that should be reported and for which there are legal restrictions on driving was also poor in this study. For example, although most knew that epilepsy was a condition patients should report, only 9 knew the correct driving restrictions; 30 of the 50 doctors knew that myocardial infarction should be reported, but only 5 knew the correct restrictions; only 21 knew that diabetes should be reported (8 of these knew the correct restrictions).

Other studies have found slightly better results (e.g., O'Neill, Crosby, Shaw, Haigh & Hendra, 1994, cited in Kelly et al., 1999) for some conditions, but only when the information was requested by post, rather than in the realistic, unprepared situation described by Kelly et al., and have found similarly low levels for the same common conditions as found by Kelly et al., e.g., 35% correct knowledge for uncomplicated myocardial infarction. On the same question of advice needed following a myocardial infarction, in another postal study, King, Benbow and Barrett (1992) found a difference between hospital doctors and GPs. In this study, 30% of hospital doctors and 59% of GPs answered correctly. This study did have a rather lower response rate than other studies (32% of hospital doctors and 26% of GPs), but generally found that GPs' knowledge of the issue was better than that of the hospital doctors. Another postal study by Gillespie and McMurdo (1999) surveyed all consultant members of the British Geriatrics Society, receiving a 59% response rate. Of the respondents, only 67% knew that drivers had to re-apply for a driving licence at age 70, but most (83%) knew that they could legitimately breach patient confidentiality to inform the DVLA if the patient was incapable of understanding advice that their condition was likely to make them a danger at the wheel. Most also knew that their main role was offer advice and information regarding driving rather than to enforce regulations, and that the responsibility for informing the DVLA about medical conditions lay with the patient in most circumstances. This study found that the geriatricians'

knowledge of DVLA advice on specific conditions was uneven – for example, 51% would not have advised patients with non-sustained ventricular tachycardia to suspend driving or to inform the DVLA for assessment, contrary to DVLA recommendations, but most would correctly not advise patients with an existing fully functioning pacemaker to give up driving (DVLA recommends suspension of driving for four weeks following fitting of pacemakers).

Finally, Kelly et al. found that only one of the doctors interviewed in their study knew where to get the appropriate information if they did not know it (i.e. from the DVLA). While not all groups of doctors may fare as badly as the groups in these studies, they suggest that such information needs greater emphasis in training. With the increasing computerisation of patients' records, software that reminds the doctor to consider and advise on driving given certain keywords in the patients' notes could be envisaged. Although some doctors are reluctant to advise on driving, the increase in litigation in which doctors are held to be liable in the event of an accident for not having advised a patient to stop driving, acts as a caution (O'Neill et al., 1994). In the majority of cases, simple advice to restrict driving temporarily, or in certain circumstances (e.g., in darkness, or while on a particular medication) is enough, most people being well motivated to reduce their risk. However, very occasionally, advice to give up driving is not heeded by patients and in these circumstances the doctor should inform the patient that he/she has a responsibility to safeguard the public and inform the medical adviser at the DVLA, being within his/her rights to breach confidentiality where the public at large may be placed at risk. In these circumstances, the procedure is that doctors inform the patient that they must report their 'driving contrary to advice' to the DVLA, before doing so.

Generally, evidence suggests that people restrict or give up driving in a sensible manner as their awareness, for example, of failing eyesight impinges (e.g., Rabbitt, Carmichael, Shilling and Sutcliffe, 2002), but many people (some of whom give up unnecessarily) can be helped to maintain driving (and therefore all the mobility benefits that gives) by careful planning, for example, to avoid certain conditions, such as poor visibility or rush hour.[1] It is generally agreed that older people are at more risk as pedestrians than they are as drivers (Mitchell, 2000).

3 Age-related changes as they affect driving ability

A full description of motor, sensory and cognitive changes as they affect driving can be found in Holland (2001). References to other specific reviews are provided in these paragraphs. The age-related changes are, in summary:

Movement and motor changes

A salient difficulty older people commonly suffer from is muscle and joint stiffness, which may prevent the older driver from easily turning the head and body to look to the rear, and may affect the ease and frequency of head movements which are usefully made to monitor position in dense traffic and reverse safely.

Eye muscles commonly atrophy with increasing age and as a consequence, older people become less able to raise their eyes to the same extent as a young adult, and become much slower to make eye movements to fixate objects of interest. This leads to a more 'static' head with consequent loss or imprecision of monitoring of peripheral information, which is a salient characteristic of older drivers.

Goggin and Stelmach (1990b) reported that older people show planning deficits in both the preparation and the maintenance of preparation of movements, difficulty in programming or in reprogramming a response, and control problems in the execution of movements. In particular, these authors concluded that older people do have difficulty maintaining preparation over longer intervals, and questioned whether this could really be attributed to general slowing as many researchers assume, but rather, suggested that it may be due to specific ineffective movement control processes (see also Goggin, Stelmach & Amrhien, 1989).

Generally, the evidence points to the findings that older people are not slower at movement itself, but at making the decisions about movement selection, changes and the fine motor planning required, for example, they move towards a target at the same speed as younger people, but slower as they approach the target. Older people show less ability to scale their movement velocity to the amplitude of the movement, for example, going faster for long movements. Older people also decelerate for longer as they reach a target (Goggin and Stelmach, 1990a, cited in the review by Stelmach and Nahom, 1992). Further details can be found in the review by Stelmach and Nahom (1992).

Decline in vision and perceptual abilities

- Static and dynamic visual acuity declines, particularly acuity in poor light.

- Dark adaptation takes longer and does not reach the same level as found in younger adults.

- Increased sensitivity to glare, and increase in time taken to recover from glare.

- There is reduction in both horizontal and vertical visual fields (i.e. reduction of ability to see things in the periphery of the visual field).

- Mild changes in the efficiency of colour vision in old age.

- Reduction of light entering the eye and reaching the retina.

- Loss of spatial frequency sensitivity (loss of resolution of 'fine grain' information, specifically affecting speed and distance discriminations).

- Reduction of flicker fusion frequency – threshold at which a person can detect that a light source is not constant.

Further details can be found in reviews by Corso (1981); DLTR (2000b), Panek, Barrett, Sterns & Alexander (1977); Fozard (1990) and Schneider & Pichora-Fuller (1999).

Effects of these changes in efficiency of sensory systems

The quality of the information older people can get from the environment is often inadequate and downgraded, thus increasing the probability of errors and misjudgments. In the context of driving the main effect of sensory losses is the dramatic increase in time and effort to make perceptual discriminations. The effects of this on performance may be quite severe, and when other conditions, such as poor lighting make discriminability of other traffic, of signals and of signs more difficult, the concomitant results on older people may be serious. Losses of sensory discrimination will have real practical consequences when the information to be registered is complex, for example, some directional road signs. Consider, also the person with a small reduction in visual acuity who needs to be closer to an overhead sign in order to read it, but when near enough to read it, proximity to the overhead gantry means that eye and head movements are necessary. A small reduction in speed of information processing may additionally mean that the sign is simply not visible for long enough for the required information to be extracted. There is evidence that decline in sensory function shows an increasing relationship with decline in cognitive function with increasing age (Baltes, Staudinger & Lindenberger, 1999).

Decline in cognitive capacities

The two most important overriding factors in ageing cognition are: (i) The variability of performance, both between, and within individuals, increases with increasing age. (ii) The speed of processing of information reduces, with a corresponding reduction in the amount of processing that can be conducted at any one time (see Perfect & Maylor, 2000, for a discussion of these issues).

Thus it can be seen that the effects of declines in both vision and in cognition result in a slowing of processing, decision making and reaction. Importantly, these two factors interact:

That is, an equivalent decline in visual acuity brings about a much greater increase in decision time in an older-old than in a young-old population. Younger people have more central perceptual computing power to bring to bear to resolve perceptual deficiencies than do older people who consequently do not cope as well. Rabbitt (1991) has shown with hearing that mild difficulties that do not prohibit accurate recognition of information, nevertheless reduce memory for the information and making of appropriate implications from it (i.e. people do not process it as well) and that this effect is greater for older people, especially those with lower fluid ability – (e.g., as measured by I.Q. tests or tests of reasoning ability), i.e., those with a decline in their general processing resources. Indeed, similar studies with younger people with visual or auditory difficulties simulated to match impairments found in normal ageing have found no such impairment of cognitive processing of information (e.g., Lindenbeger, Scherer & Baltes, 2001) suggesting that younger people are able to devote more attention to processing information where they perceive there is a deficit, but older people may not have the spare capacity to do this.

Thus, old age also attenuates the global information processing resources that people can deploy to analyse and interpret sensory information. The increased information processing demands of dealing with degraded sensory information can use up attenuated resources so as to deprive older people of the additional capability needed to accurately analyse and react to information they have extracted.

Changes in attention

- Selection of critical from irrelevant information

Older people scan the environment much slower than younger people. The larger the number of different objects or targets for which search is conducted, the longer the search takes (for everyone) – multiplication by a constant of 1.5 per item will produce reliable approximations for older adults (Cerella, 1985).

There are important age reductions in the size of the 'functional visual field' (Useful field of view (UFOV) – Ball et al., 1988). Individuals who show functional narrowing in this measure of peripheral visual attention have been shown to have more accidents. Measures of selective attention are the most reliable predictor of accident risk as compared with other measures of attention and the older the study population, the higher the correlation between measures of selective attention and accident rate (Parasuraman and Nestor, 1991).

- Divided attention – Changes in ability to do two things at once

Older people have difficulty carrying out a simple ballistic movement at the same time as processing information necessary to guide its termination. Inability to take in information and manoeuvre at the same time is a characteristic of 'older road user' accidents – collisions at slow speeds on roundabouts or right turns at junctions crossing oncoming traffic are common.

- Speed and efficiency of alerting – the time course of expectancy

Learning to correctly anticipate is perhaps the core of driving skills:

(i)   Older people can and do make correct anticipations and benefit from them. Indeed, they gain even more than the young from ability to make correct anticipations, i.e. the difference between alerted and unalerted reaction times is greater for older drivers than for the young – although this does not mean that the old can then respond as fast as the young. Older people respond very slowly indeed when not given any advance information to enable them to prepare. Probably the gains made when alerted are proportional to older people's longer RTs.

(ii) Older people take longer to build up successful anticipation. For advance information to work for older people it must be given slightly longer in advance.

(iii) Older people are much slower to recover from incorrect anticipation, probably in a way that is disproportionate to their slower reaction times.

- Sustained attention (vigilance)

Older people show little difference from the young in simple tasks, but in more complex tasks with poorer signals or heavy signal load, where the use of working memory is needed when events unravel over time, and where they are expected to maintain a high rate of information processing, older people are more likely to make isolated responses which are 1.5 to 2.0 standard deviations slower than the rest of their responses, known as blocks. Older people make more of these blocks, and individuals with higher IQ (greater information processing resources) make less of them.

For literature reviews of attention in old age, see Hartley, (1992) and McDowd & Shaw (2000).

Self-monitoring and detection of errors

People do become less sensitive to changes in their own performance and capacities (e.g., Rabbitt and Abson, 1990). This is due to their changing, generally less taxing environment, but also to the reduction in information processing capacity, which means that feedback is not always monitored at the same time as completing the task at hand. Older old people are increasingly less able to monitor their own performance – to notice when they have come near the bounds of what is acceptable or risky. For example, Rabbitt (1990) found that older people were less likely to remember errors or to signal errors.

Finally although age-related changes are often small, they can be very interactive so that a combination of many slight changes can result in marked changes in efficiency.

Importantly, older people have less reserve with which to compensate for small changes in vision, motor strength etc. They have lost the speed with which to recover from lapses.

4 Increased risk of road traffic accident in various disease states

4.1 A 'severity of all combined effects' approach

The most important thing to bear in mind when considering unwelcome effects of drugs in older people is the basic fact that the person taking such medication is unwell and needs the drug therapy, and that the effects of the medicine is only one contributor to the pattern of influences that affect a person's safety as a driver, for example, effects of their illness or illnesses, combined with other age-related changes in function.

The key point to consider throughout this section and subsequent ones is not whether a particular illness or drug may generally have an effect on driving performance, but rather, whether individual patients are capable of functioning safely in the environments to which they expose themselves. That is, the combined effects of ageing, illnesses and medication mean that making a judgment as to whether someone is fit to drive based only on the diagnostic category of their illness or even on one or more categories of medication they are taking is inappropriate. Many other factors also need to be considered, particularly in older people where comorbidity of several disease processes, and polypharmacy are particularly common, in addition to normal age-related changes in vision, speed of information processing and reaction, musculo-skeletal mobility and strength. As Dobbs, Heller and Schopflocher (1998) stated in relation to older drivers:

> 'The number of possible interactions among illnesses, severity levels, drug treatments and dosages is too large to make it practical to develop a compendium of conditions and drugs for physicians or others to use as a "look-up" table for predicting an individual's driving competence' (p364).

The important issue is to determine whether a person is capable of driving safely, that is, their net driving function is what should be considered, rather than each specific condition (e.g. Waller, 1965). Wallace (1989 – cited in Waller, 1992) also noted that changes in functional abilities as a result of normal ageing or as a result of disease-related pathology should not be distinguished because 'the end point, rather than the source of functional loss is of concern' (1992, p5). Retchin (1989) also noted that functional status should be assessed as a net effect of all of the physiological and pathological forces that may be acting at any one time, rather than as a function of a specific diagnosis in isolation, and that this approach is especially important when considering older drivers. We need to be aware that a person with one illness may also have other significant illnesses or symptoms, or, for example, that the functional effects of an illness may be exacerbated by depression, or alcohol or a combination with age-related functional impairments, e.g. in visual abilities. Studies examining effects of comorbidity of diseases are not common in relation to driving, but Naughton, Pepler and Waller (1982) found that among older drivers hospitalised for ischaemic heart disease, 41% also had hypertension, 23% had lung disease, and 10 to 15% had arthritis, diabetes, depression, alcoholism or cerebral vascular disease (cited in Waller, 1992). One study that did examine combinations of illnesses in relation to driving risk is

that by Koepsell, Wolf, McCloskey et al. (1994). They examined the combination of diabetes and coronary heart disease and found that this combination resulted in a much higher risk (using odds ratios (OR) as a measure) of sustaining a motor vehicle collision injury (OR = 8.0); the increased odds ratios over people without the illness when considered separately were much lower than this (OR for diabetes was 2.6, and that for coronary heart disease was 1.4).

There are also problems of control when attempting to examine any increased risk associated with specific illnesses: People with chronic illnesses may change their driving because of their illness, thus making an assessment of real risk difficult as compared with healthy drivers. For example, Stutts (1998, cited in Lyman, McGwin & Sims, 2001) found that older people who drove less than 3,000 miles per annum were more likely to have visual impairments and Waller (1987, cited in Waller, 1992) found that people with severe heart disease were more likely than people with less severe heart disease or without heart disease to reduce their annual mileage generally, but also were more likely to make specific changes to their driving such as reducing driving in bad weather, at night or at high speed. Rabbitt, Carmichael, Shilling and Sutcliffe (2002) reported that older drivers with high scores on a self-rated measure of health, indicating a greater number and severity of symptoms and illnesses (the Cornell Medical Inventory – CMI), reported significantly lower annual mileage than older drivers with lower scores on this measure. Importantly, this relationship was also found longitudinally, such that increases in CMI scores over a three year period reliably predicted reductions in mileage. That this finding was not a simple function of people reducing mileage with increasing age was suggested both by a lack of reliable relationship between chronological age and change in mileage over the three years of the study (Rabbitt et al.'s Table 2.3), and also by the fact that people who reported fewer illnesses and symptoms (lower CMI scores) at the later date than they had done three years before, had actually increased their mileage.

Another study by Lyman, McGwin and Sims (2001) examined associations between self-reported illnesses or impairments and driving frequency and mileage among older drivers. They found that people with difficulties in activities of daily living such as dressing or feeding drove less often, as did people reporting mobility difficulties, such as using stairs or walking a quarter of a mile. People with low annual mileage were more likely to be suffering from cataracts, high blood pressure or kidney disease, be cognitively impaired (as measured on the Short Portable Mental Status Questionnaire, SPMSQ; Pfeiffer, 1975) and have poor far vision. Thus an examination of the relation between illnesses and accident rates is likely to be an underestimate of the real effects of the illness on driving since people with such illnesses as those indicated sensibly reduce their driving, and thus affect their likelihood of an accident. This is an important explanation for the often found differences in correlations between an illness or a medication and on-road or simulator driving performance and that between the same illness or medication and actual accident data, correlations often lacking or being smaller in the latter comparison, as a result of such reductions in driving and compensatory driving pattern changes made for perceived difficulties by the older person. However, such reduction of driving implies a reduction in mobility and a possible increase in pedestrian risk, and so treatment and rehabilitation of the difficulties causing such reduction in driving is needed – for example, treatment for cataract

restores visual function well. Some older people may be reducing driving overall, when only a reduction in certain circumstances (e.g., at night) is merited by their condition and specific advice on kinds of driving to avoid would enable their mobility.

It is thus more appropriate in considering what advice to give to an older driver to have in mind a 'severity of all combined effects' model, rather than a particular diagnostic group or drug classification. It is the end functional ability that is of central importance.

The questions that follow such a statement, in practical terms are:

(i)   How does one identify a patient for whom driving may have become a problem? This document sets out some of the major sources of difficulty that may be reducing driving safety in a patient, that is, illness and medication effects, and summarises other normal age-related changes. These general difficulties are reviewed in full elsewhere (motor and visual declines, normal age-related cognitive declines – Holland, 2001). Another major source of information that may raise the concern is that worried relatives often approach a GP for advice, and this is especially important if the family relays specific anecdotes that illustrate a real glaring safety threat. Some particular incidents that are indicators of serious potential risk are: arrhythmias (e.g., Gresset and Meyer, 1994), syncope or dizziness while sitting or lying (e.g., Rehm and Ross, 1995; Waller, 1967), seizures (e.g., Taylor, 1995; Hansotia and Broste, 1991), severe or frequent incidences of hypoglycaemia in diabetics (e.g., Frier, Steel, Matthews et al., 1980; Koepsell, Wolf, McCloskey, Buchner, Louie, Wagner & Thompson, 1994), serious memory loss, getting lost in familiar surroundings, and episodes of acute confusion. A useful summary of appropriate assessments and indications of unsafe driving is also found in Foley and Mitchell (1997).

(ii) How does one know if an unwell or medicated person is actually fit to drive or not? Most medical practitioners do not have time in their appointments system, nor the expertise, for any more than basic screening. A first point to consider is basic visual abilities, and screens for extreme visual difficulties, for example, monocularity or very restricted visual acuity are quickly done in a surgery setting, but GPs often advise patients to go to their optician for detailed visual screening. The different visual abilities and their association with driving are reviewed and examined elsewhere (e.g, Holland, 2001; DLTR (2000b), Panek, Barrett, Sterns & Alexander, 1977).

The following are some examples of relatively simple screening tests available that could be administered in a GP surgery setting, either by the patient themselves or a practice nurse. Others are mentioned in relation to specific studies, for example, in sections on Stroke or Dementia below. Some, such as the Mini Mental State Examination (MMSE) are already in habitual use by GPs and Geriatricians in general terms, and their relation to driving is referenced here. Some, such as Activities of Daily Living measures (ADL) are of particular use in giving advice following an acute episode of illness, for example, following a stroke.

SAGE Older driver screening programme: This can be recommended to a patient by a doctor, but is administered by SAGE and the patient themselves. It includes driver assessment (with a driving instructor), vision screening and medication and general health

review. Gloucestershire County Council, Road Safety Team, Environment Department, Road Safety Unit, Shire Hall, Gloucester GL1 2TH. Cost: approximately £15 to the patient, but carries with it a discount on car insurance with certain providers.

Useful field of View (UFOV[(R)]) test. Computerised test of peripheral visual attention, with much accident risk related validation with older drivers (e.g., Owsley, et al. 1991). This involves the purchase of an expensive piece of computerised equipment, but once available, this costs only the time of a tester. Further details available from Kristina K. Berg, Visual Resources Inc., (312) 454-0603m757 W. Diversey, Chicago, IL 60614.

Activities of daily living (ADL measures – Various, e.g., Katz, 1983, which focuses on physical ADL; Duke OARS multidimensional functional assessment questionnaire, 1978, which focuses on Instrumental ADL). Relationships of such measures with crash incidence reported in NHTSA Report No DOT-HS-807554, (1989) cited in Owsley, McGwin and Ball (1998).

Mini-mental state examination (MMSE – Folstein, Folstein & McHugh, 1975) relationship with on-road performance measures found by Fitten et al., (1995), see details below in Secion 4.2.5.1 on dementia.

Motor ability: simple tests of strength or range of movement can be done in a surgery setting if a patient or doctor is concerned about effects of movement symptoms on driving. Patients can be referred to Disabled Drivers' Assessment Centres for detailed assessment and advice on vehicle adaptations that would enable them to continue driving safely. These centres are listed in Medical Aspects of Fitness to Drive (see above).

Drivers 55 plus: Check your own performance – an American self-assessment, with good advice that patients can take away and do themselves, and perhaps discuss the outcome with their doctor. Available free, orderable from the AAA Foundation for Traffic Safety website.

A person giving advice may wish to consider each of the following five areas, and importantly, potential interactions between them, in terms of whether the older driver has difficulties in each domain, and how serious each difficulty is, as a guide to whether further advice or assessment by other professionals is indicated:

(i)   Difficulty with movement of motor control

(ii)   Impaired visual abilities

(iii)   Impaired cognitive factors

(iv)   Diagnosis and severity of illness

(v)   Type of drug therapy.

It is suggested that a serious difficulty or possible effect on driving in any one area may mean that driving is too risky, at least for the time being, but, more commonly, that minor effects in more than one of these areas will combine to reduce the driver's 'reserve capacity' for coping with demanding or unexpected driving situations, and may also mean that driving is too risky, at least for the duration of a prescription or illness, or that further detailed assessment is needed.

4.2 Risks associated with specific illnesses

Bearing the above caveats in mind, we will now go on to examine a series of diagnostic groups of illnesses and specific illnesses in the context of observed changes in driving performance, and importantly, crash risk. It is emphasised that this is not intended to be a complete survey of all illnesses that may have any effect on driving in older patients, and that any illness, whether featured here or not, may have a direct or indirect effect on driving related processing. The illnesses featured are selected because they are increasingly common or their effects are increasingly severe with older age, perhaps because of their combination with effects of normal ageing, and also because they have been specifically researched in relation to driving. Diagnostic groups of illnesses are set out in the order they appear in the British National Formulary, in order to be compatible with drug information (Section 5). Some diagnostic categories are omitted, largely because relevant research was not found or this particular category was not subject to a literature search because of limited relevance (e.g., obstetrics, gynaecology and urinary-tract disorders). Where possible, direct evidence of accident risk is given priority, followed by evidence from on-road driving tests. In some cases, it is useful to consider performance on neuropsychological tests, simulators and 'off-road' driving test-tracks, particularly in situations where prediction of safe driving is necessary before on-road driving could be resumed, for example, after a stroke.

4.2.1 Gastrointestinal system

This review did not find any particular evidence for gastrointestinal disorder affecting driving safety. Even extensive surveys that included a variety of common illnesses, such as that by Koepsell, Wolf, McCloskey, Buchner et al., (1994) did not include gastrointestinal disorders. One indirect study which examined effects of different medications on relative risk of having an accident included gastrointestinal agents, and therefore, by implication, patients with gastrointestinal disorders (Foley, Wallace & Eberhard, 1995). Foley et al. found a non-significant increase in relative risk of accident for those taking such medications. However, the general advice of avoiding driving while feeling particularly unwell or uncomfortable, particularly if the condition may cause sudden distracting symptoms or pains, is important.

4.2.2 Cardiovascular system

Crancer and O'Neall (1970 – cited in Waller, 1992) found an almost doubled crash incidence for drivers known to have heart disease. These were patients known to motor vehicle agencies because of their condition and may have therefore been more seriously ill than people with cardiovascular diseases not known to such licensing agencies. Not all such crashes have obvious clinical incidents related. Nevertheless, there are subtle alterations of function with many medical conditions that may affect driving – for example, subclinical electrocardiographic changes have been observed among persons with heart disease associated with driving in heavy traffic (Bellet, Roman, Kostis & Slater –1968, cited in Waller, 1992). The most dangerous situation is for people whose illness causes fluctuation in cognitive function or arousal.

In a study of 2,000, acute collapses at the wheel while driving and leading to police reported accidents involving personal injury, Taylor (1983) showed that only 10% were due to coronary heart attacks and 7% to stroke, the rest being due to epilepsy and diabetic hypoglycaemia. Cardiovascular disease accounts for approximately half of all deaths in the UK and approximately one quarter of all deaths are due to coronary heart disease (Taylor, 1995). Taylor (1995) noted that although death is commonly sudden, heart disease is a fairly rare cause of road traffic accidents – since medical details of such deaths when observed in coronary care units suggests that death is sudden, but not instantaneous. That is, drivers may have a brief moment in which to pull to the side. Taylor cites Christian, (1988): 'a driver was commonly found dead at the wheel of his vehicle beside the road, with the engine still running' (Taylor, 1995, p31).

Associations of road accidents with coronary heart attacks is only a small proportion of the potential influence of cardiovascular diseases on driving performance and the increase of such accidents for people with cardiovascular disease is not necessarily related to actual 'clinical episodes' such as heart attacks (Waller & Goo, 1969, cited in Waller, 1992). In general, studies which have asked accident involved drivers about illnesses have asked whether or not they have experienced a heart attack or give only a very general classification such as the presence of 'cardiac disease' (e.g., Rehm & Ross, 1995; McGwin, Sims, Pulley & Roseman, 2000), but some have asked for more details and explored a greater variety of function or symptoms, and these are perhaps more informative as we seek to determine whether cardiovascular disease, or which components of it, have an influence on driving risk. One such study is that by Koepsell et al., (1994) who examined risk of crashes associated with a variety of conditions, including history of heart attack, angina pectoris (chest pain), bypass surgery, pacemaker and 'any coronary health disease'. Koepsell et al. found that the general measure of any coronary disease, and having angina both significantly increased the likelihood of being involved in an accident. Their results for presence of a pacemaker were suggestive of a relationship, but they had very few such patients and so statistical significance was not achieved, and further research on this group would be needed.

Another approach is to examine the relationships between symptoms and crash risk, rather than actual diagnosis, and this is the approach taken by Foley, Wallace and Eberhard (1995). They found a significant increase in crash risk for drivers reporting chest pain, supporting the findings of Koepsell et al. on risk associated with angina. In a study examining 70-year-old men in Quebec, Gresset and Meyer (1994) were able to use medical information from a statutory medical examination that all drivers in Quebec have to undergo in the 6 months prior to their 70th birthday in order to renew their licence when they turn 70. 1,400 drivers who had an accident as a driver in their seventieth year were then examined in relation to their medical report. Only accidents resulting in property damage or mild injury (not requiring hospitalisation) were included. This strategy has the advantage of controlling for the increased frequency of injury in accidents involving older people due to their physical frailty rather than the actual severity of the accident, but it does have the disadvantage of reducing the number of accidents included. Nevertheless, this strategy only excluded 3.6% of accidents to male drivers in their Seventieth year. Gresset and Meyer calculated odds ratios for the likelihood of accident for each of a series of medical conditions, compared

with people of the same age who were not involved in crashes. They included any type of heart disease as one category, but also broke this down into heart failure, hypertension, arrhythmias and ischaemic heart disease. Although all these conditions slightly increased the odds ratio of having had an accident, the differences were not statistically significant. Only presence of arrhythmias significantly increased the odds ratio. Such findings illustrate that studies which separate out different symptoms within the classification of cardiovascular diseases will give us a clearer picture of increased risk than studies which consider cardiovascular disease as one category.

Overview

A key point is that the relationship of road accidents with actual coronary heart attacks is only a small component of the total relationship of cardiovascular illness with driving risk. Studies which have separated out different cardiovascular conditions have indicated that some conditions or symptoms are more associated with having a crash than others, and key examples are cardiac arrhythmias and chest pain.

4.2.3 Cerebro-vascular disease (Stroke)

Stroke is defined as 'sudden, spontaneously occurring disturbances of the brain following arterial occlusion or intracranial bleeding' (Lings & Jensen, 1991, p74). Driving after a stroke is problematic if there are cognitive changes, even assuming that the patient is physically rehabilitated enough to manage the driving task. Many people do not resume driving after a stroke. For example, in one survey of 144 stroke victims who had been drivers before their stroke (Legh-Smith, Wade & Hewer, 1986), 58% had not resumed driving one year post-stroke. This study found that those who had not resumed driving were generally older than those who had, and that they were more likely to suffer from other illnesses that restrict driving, such as epilepsy, and be more functionally impaired than those who did resume driving. In another such study, Nouri (1988, cited in Fisk, Owsley & Pulley, 1997), found that 50% of stroke patients who had been drivers before their stroke had resumed driving by a 6 month post-stroke check-up. In a careful study which excluded any patients with two-sided cerebral effects of stroke, or complications such as visual disturbances or a variety of other disease processes, and which also selected for age under 70 (although they did include some patients over this age) Lings and Jensen (1991) found that more than 70% of their patients had resumed driving. In another study of 290 stroke survivors, only 30% had resumed driving (Fisk, et al., 1997) when surveyed, although in this study the survey point was between 3 months and six years post-stroke. In this study, increasing age was associated with reduced likelihood of resuming driving after a stroke, and people who had not resumed driving were more disabled on a number of physical and cognitive indices than those who did resume driving. In Legh-Smith et al.'s study, stopping driving was associated with a loss of social activities and with a higher frequency of depression, even despite easy access to alternative car transport (28% had easy access to car transport within their own household, 51% had easy access from outside their own household). These authors suggested that some patients experiencing difficulties could be assisted to resume driving safely if they were offered re-training or assessment for vehicle adaptations, and thus maintain their independent mobility. In Fisk et al.'s US study (1997),

48% of patients reported that they had received no advice about driving during their rehabilitation, and 87% reported that they received no driving evaluation. A study conducted in the UK by Simms (1992) found that 70% of the less competent drivers (those who failed the driving test in the study) who had suffered a stroke had arranged driver retraining before resuming driving, as compared with 48% of the post-stroke drivers who passed the driving test. That is, those who perceived themselves to be likely to experience difficulties often arranged retraining for themselves.

Simms (1992) study compared recovered stroke patients with age, sex and driving experience matched controls. Matching on current driving experience was attempted, but although the range of mileages was similar between the stroke and control drivers, in reality, the average mileage of the control drivers was almost twice as far as that of the stroke patients. Although statistical difference testing was not reported in this study, figures show little difference between stroke patients and controls in terms of failure rate on a driving test, 20% of the patients and 24% of the controls failing the test. However, Simms did find an increase with age in both groups in failure rates, and found that older people, particularly those who had suffered a stroke, were more likely to restrict their driving, for example, they were less likely to drive on motorways, unaccompanied, at night or abroad.

Studies of the relationship between stroke and accident generally investigate effects of driving after a stroke, but Taylor's study of acute collapses at the wheel found that 7% were due to stroke. Studies specifically examining accident likelihood in older drivers following a stroke are less common than studies examining accident risk in other medical impairments, but there are many papers examining relationship of a range of medical conditions (including stroke) to accident frequencies, and by virtue of the fact that stroke becomes more common with increasing age, many of these papers include older patients. One that included paralysis in their analysis was the study by Gresset & Meyer (1994) detailed above. Although of limited use since they did not separate out paralysis into that due to stroke from that due to other causes, and gave no indication as to the severity or location of the weaknesses, this study did find a moderate increase in odds ratio in 70-year-old men who had had an accident as compared with those who had not had an accident. McGwin et al., (2000) compared the odds ratio of having an accident in which the older driver was at-fault with that of accident involved older drivers judged not to have been at-fault (as compared with non-accident controls). The odds-ratio for stroke was significantly elevated for 'at fault' drivers but not for 'not at fault' drivers. An innovative study by Haselkorn, Mueller & Rivara (1998) compared accident and traffic violation rates for different groups of patients after hospitalisation for traumatic brain injury, stroke (CVA), extremity fractures or appendicitis with age, sex and 'zip-code' matched controls, carefully adjusting for prior driving record. Results did not support the hypothesis that brain injury led to an increase in accidents or traffic violations, there being no increase in relative risk for the brain injured groups in the 12 months after their hospitalisation. There was a modest increase in relative risk of traffic citation for patients who had suffered a traumatic brain injury and those who had suffered an extremity fracture, suggesting that this increase may be due to personality characteristics such as risk taking behaviour, rather than after effects of injury. Simms' (1992) study found that despite increased errors among stroke patients in driving, such as errors at junctions and in awareness of traffic situations, there was no difference from

controls in numbers failing a driving test, and none of either the stroke or control group (50 people in each group) had experienced a major accident or a two-car collision in the previous year. However, older stroke patients (over 70s) reported twice as many minor incidents, such as scrapes, broken mirrors, backing into gateposts, than did same age controls, and the author suggests that many of these seemed to have occurred in the period immediately following resumption of driving.

Other studies have examined stroke as one of a number of medical conditions in a general sample (e.g., Sims, Owsley, Allman, Ball & Smoot, 1998) and numbers of stroke patients have been too low for any meaningful analysis. However, in a well-controlled study by Hu, Trumble, Foley et al., (1998), none of the commonly studied medical conditions, such as heart disease or stroke were associated with increased crash risk, and the authors suggested that functional impairment, rather than actual diagnosis, is the key factor to consider in future studies.

Actual function is the central focus of most of the large number of studies that specifically examine driving ability after a stroke, with driving-related, laboratory based psychomotor and cognitive assessments often being compared with on road and/or simulator driving assessments. Studies that have examined the driving of stroke patients (e.g., Wilson & Smith, 1983; Simms, 1992) have found that, compared with controls, recovered stroke patients seemed to have difficulty entering and leaving motorways and making judgments of traffic at roundabouts, and that some patients have particular difficulty with awareness of other road users and at junctions. Wilson and Smith also reported other findings that would be expected if the cognitive resources of the patients was depleted by their stroke, that is, reduced awareness of other vehicles, difficulty responding quickly to emergencies and difficulty doing two things at once. Nouri, Tinson & Lincoln (1987) conducted a detailed analysis of the relationship between laboratory cognitive tests and on-road testing post-stroke and identified 10 tests that together discriminated between those who had passed the driving assessment and those who had failed in 94% of cases, although a rather small number of patients were used for such a validation (40 patients). Nouri & Lincoln (1992) attempted to further validate these tests on a further group of 40 stroke patients, combining results from the two studies resulting in 79 patients' assessments on those tests that the first study identified as discriminatory between those who passed a driving test and those who did not. Although most of their tests differentiated those who passed or failed the driving test, the authors identified three cognitive tests (Dot cancellation, road sign recognition and 'what else is in the square' testing concentration, spatial reasoning and visual perception – see paper for details) that together predicted the road test performance of 81% of their stroke patient participants. A study by Mazer, Korner-Bitensky & Sofer (1998) examined a series of perceptual-cognitive tests in terms of ability of the tests to predict actual driving performance. The rationale of such studies is to determine whether any such perceptual-cognitive tests predict driving performance well enough for them to be used as screening tests to determine which stroke patients are not, at present, suitable for an on-road driving test. Mazer et al. found that the two tests with the highest predictive values of passing and failing the driving tests were visual perception tests used widely in clinical settings in the USA called the Motor Free Visual Perception Test (MVPT – Bouska & Kwatny, 1982) that measures perceptual skills in five areas: spatial relations, visual discrimination, figure

ground discrimination, visual closure and visual memory, and also the Reitan Trail Making test (B) (Reitan, 1986). Importantly, these authors found that the tests were better predictors of those who failed the driving test than of those who passed, in that patients who performed poorly on both these tests were 22 times more likely to fail the driving test than patients who performed well on these tests. These authors were also careful to examine left and right-sided lesion stroke patients separately, finding that the Trail making (B) test was the best predictor for patients with left-sided lesions, and the MVPT for patients with right-sided lesions.

Of particular relevance for the driver are the movement and strength impairments associated with the common hemipareses associated with stroke. However, some authors have suggested that physical limitations and movement difficulties are less of a barrier to driving than more central impairments such as poor perceptual or cognitive skills. For example, Sivak, Olson, Kewman et al., (1981), cited in Kumar, Powell, Tani, Naliboff & Metter (1991), found that motor-impaired patients with spinal-cord injury did not differ from controls in driving skills, and that certain neuropsychological tests correlated well with driving performance (tests used were components of the widely used WAIS intelligence test: e.g., picture completion and picture arrangement). Kumar et al. took this question further by examining differences between recovered stroke patients who could be retrained for driving and those who did not succeed in obtaining a driving licence after their stroke. They further divided those who drove into those who drove unrestricted on busy streets, on freeways (motorways) and in unfamiliar surroundings, and those who drove in a more restricted manner, avoiding unfamiliar areas, avoiding freeways and busy times or difficult weather conditions. The latter driving group had needed more retraining before they had passed their post-stroke driving test, and differed significantly from the unrestricted drivers on the WAIS neuropsychological tests, but did not differ significantly on these tests from those who had not passed their driving test. This is a finding worth noting, since it shows that some of the group of patients who perform poorly on the cognitive tests that are shown to be related to driving, can be retrained to drive without incident, and that restrictions such as avoiding certain fast or complex situations are sensibly self-imposed by these drivers. The researchers found that none of the restricted driving group had experienced an accident or received a traffic citation during the two years following their re-licensing. In Simms' (1992) study of older drivers, including people who had resumed driving after their stroke, both stroke patients and controls who failed the study's on-road driving test had a lower annual mileage than those who passed. However, although the study does not report statistical significance, only the difference in mileage between the passed and failed stroke patients appears substantial, stroke patients who passed the driving test having twice the mileage, on average, of those who failed. Simms also found that more of those who failed the test in the study reported avoiding driving alone, on motorways or at night, with there being a particular difference between those who passed and failed for the stroke patients in terms of driving alone or at night.

Lings & Jensen (1991) found that reaction times were longer for patients than for controls in a simulator driving test, both for the paretic and contralateral extremities, particularly for people with right-hemisphere damage, suggesting a more central cognitive origin of this slowing of response, perhaps associated with activation of attention. In addition, 22% of patients with left-sided paresis and 30% of those with right-sided paresis made at least one

failure to react at all to a traffic light or auditory signal, an error that did not occur at all in the control group. They also found that directional errors were more common for people suffering from right-sided paresis (left-hemisphere strokes). However, Lings and Jensen also explored the effect of fitting a central pivotal steering knob on the steering wheel of their simulator vehicle enabling operation with one hand only. They found that in many cases, times to make steering movements in reaction to a directional signal were normal with this aid, where they had been much longer than times of control participants with the normal steering wheel.

In addition to the physical difficulties of paresis and to the general cognitive slowing commonly found in such patients, also of importance are findings of lateral neglect of the visual field in which information from one side of the visual field is not attended to (e.g, Robertson, Tegner, Goodrich, & Wilson, 1994). A single-patient study by Barrett, Schwartz, Crucian, Kim & Heilman (2000) illustrates the care that is needed in assessing stroke patients. In this case, a woman who had experienced a left-thalamic infarction reported that when driving she had a tendency to veer towards people or objects on the right side of the road. When tested with a common test for lateral neglect, that of ability to bisect a line accurately, she performed normally in near visual space (the usual test) but erred significantly rightward in far visual space.

Right and left-hemisphere strokes are associated with differing cognitive sequelae, but both groups of symptoms could have serious consequences for driving ability. For right-hemisphere strokes (left-sided paresis), Lings & Jensen (1991) list symptoms such as impaired spatial perception, lateral neglect and inattention and apraxia (lack of ability to imagine, initiate or perform an intended action), and for left-hemisphere strokes (right paresis) they list symptoms such as aphasias (disorders in the production and comprehension of language), notably for the driving scenario some of which include directional confusion – inability to differentiate between left and right, or even in front of or behind. Apraxias are also common, as are visual agnosias (inability to recognise and interpret visual information). Sims (1992) compared the driving of left and right-sided stroke victims and controls. She reported that the performance of those with right-sided brain damage was consistently poorer than that of those with left-sided damage, more frequently failing the driving test, and particularly performing more poorly at junctions.

Overview

In summary, simple diagnosis of having had a stroke has not been reliably shown to be predictive of increased accident risk, and functional variation between patients needs to be considered (e.g., Haselkorn et al., 1998; Sivak et al., 1981; Katz, Golden, Butter et al., 1990, cited in Haselkorn et al.). Many stroke patients recover well enough to resume driving safely. Those who do not resume driving tend to be older and/or to have other sources of impairment or disability in addition to the effects of their stroke. Cognitive neuropsychological tests have been shown to be effective predictors of driving function, although most authors, including reviewers, recommend on-road testing in addition to such

screening devices. Some patients with significant physical disabilities can be helped to drive again with the use of retraining and vehicle adaptations. There is evidence to suggest that some patients with poor performance on cognitive tests can also be retrained to drive safely, perhaps with advice to restrict their driving to known routes and low-hazard environmental conditions (Kumar et al., 1991; see also Simms, 1992, above). Some authors have suggested that restrictions such as on motorway driving or driving at night may be advisable for many stroke patients (Wilson & Smith, 1983).

4.2.4 Respiratory system

Respiratory diseases such as Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnoea (OSA) become more common with increasing age – for example, OSA syndrome has been estimated as present in up to 15% of older people (e.g., see Beebe & Gozal, 2002) and COPD is estimated as present in 5 to 15% of all adults in industrialised countries (Anto, Vermiere, Vestbo & Sunyer, 2001). Other respiratory diseases such as asthma are also prevalent, but not necessarily age related. Studies examining relationships of respiratory disease with accident likelihood or with driving skill are rare, with the exception of OSA, which is a common cause of falling asleep at the wheel, reduced alertness and reduced cognitive performance. For example, Taylor (1995) cites evidence from George, Nickson, Hanly, Miller and Kryger (1987), who found that patients with sleep apnoea have a seven-fold increase in risk of car accidents. Other studies have found a lower incidence, but an incidence of at least 2 to 3 times the accident rates of controls or of the general population seems the norm in retrospective studies (e.g, Wu & Yan-Go, 1991, cited in Teràn-Santos, Jiménez-Gómez, Cordero-Guevara et al., 1999). Teràn-Santos et al. conducted a case control study comparing accident-involved drivers at emergency treatment centres with age and sex matched controls in terms of measurements of sleep apnoea and sleepiness, excluding patients with other illnesses that may render them incapable of driving, and excluding those with injuries which may have affected their breathing. Controlling for alcohol consumption on the day of the accident, these authors found that patients with sleep apnoea had a higher likelihood of being involved in an accident than patients who did not have sleep apnoea, and the accident group included more patients with sleep apnoea than the control group. However, in this study, the sleepiness scale used (The Epworth Sleepiness Scale, Johns, 1991) did not distinguish accident-involved drivers from controls, or sleep-apnoea patients from those without this problem. This suggests that either the measure is not sensitive enough for the driving situation, or that cognitive deficits resulting from sleep apnoea, rather than drowsiness itself, is the underlying reason for the increased risk of accidents.

Some studies that include a variety of illnesses have included respiratory diseases (e.g., Koepsell, Wolf, McCloskey et al., 1994; Vernon, Diller, Cook, et al., 2002). Koepsell et al. found that neither asthma nor COPD had significant effects on the relative risk of accidents and Vernon et al. found a modest increase in relative risk of accidents for drivers who had declared 'pulmonary' disease to the licensing authority. A study that examined increase in relative risk of accident for patients taking certain categories of medicine, including 'lung medications/bronchodilators', and therefore, by implication, included those being treated for respiratory disease, is that by Foley et al., (1995). Foley et al. found that such medications

did not increase relative risk of accident at all. Foley et al. also examined the relationship of specific symptoms, rather than diagnostic categories, to increased risk of accident, and found that respiratory symptoms, such as chronic cough, wheezing or phlegm, were associated with a slight (non-significant) increase in relative risk of road accident.

There are also many studies examining the relationship of COPD or OSA to cognitive performance indices, but not in the context of road safety. This pattern is perhaps a simple result of the fact that respiratory diseases do not cause any obvious impairment to the driver, and crises such as respiratory distress are not a common cause of collapse at the wheel. However, the effects of such diseases should not be ignored, and further research, for example, on OSA as a cause of daytime sleepiness in the older population specifically, and consequent effects on driving, or the effects on driving of the cognitive decrements associated with COPD would be a way forward.

The relationship between oxygen transport or oxygen saturation of brain tissues and cognition in older adults is one that has received much discussion, with some writers suggesting that a reduction of oxygenation of the brain with age is an important contributor to age-related cognitive decline (see Holland & Rabbitt, 1991, and Etnier, Johnston, Dagenbach et al., 1999 for reviews). It follows that the disruptions to oxygen transport caused by pulmonary disorders such as the COPD group may contribute to cognitive changes, and in summary, COPD has been related to slower reaction time, for example, poorer memory, reasoning skills and complex visual motor processes (see Etnier et al. for a discussion), and to tasks that demanded flexible thinking (problem solving), the ability to think abstractly, psychomotor speed and integration of perceptual and motor information – Grant, Heaton, McSweeney, Adams & Timms, 1982; Grant, Prigatano, Heaton, McSweeney, Wright & Adams, 1987. Importantly for driving, speed and coordination of simple motor tasks were impaired in Grant et al.'s studies, and all these psychological and motor variables were related to oxygen transport measures and level of hypoxaemia, rather than to actual mechanical pulmonary function.

One particular relationship current in the literature investigating the effects of OSA and consequent sleep deprivation is that with executive function – that is, the ability to plan, develop and sustain any organised approach to problem solving, and basically to maintain or shift attention appropriately. For a recent review of the large number of studies in this area, see Beebe and Gozal (2002), but in summary, these authors report that adult OSA patients have been found to perform poorly on tests of behavioural inhibition (inhibiting inappropriate responses, avoiding distractions), on tests of set shifting (ability to change response or strategy), sustaining attention, working memory and contextual memory (remembering the temporal and spatial context of events). Importantly, Beebe and Gozal report that the pattern of cognitive effects found in untreated adult OSA patients seems different from that related to sleepiness, and that the effects correlate better with degree of blood gas abnormalities and extent of sleep fragmentation. However, they also report that medical treatment has potentially helpful effects, especially if treatment is begun early in the course of the problem.

Overview

Obstructive sleep apnoea (OSA) is a respiratory disorder which has received much attention in the context of road traffic accidents, since it is implicated as one important cause of drowsiness or falling asleep at the wheel. OSA patients do seem to have an increased risk of accident, but some research suggests that this may be more related to the cognitive effects of reduced oxygen saturation in the brain than to actual drowsiness. This has important implications for other disorders, such as COPD, in which oxygen saturation or transport to the brain is impaired. The cognitive deficits demonstrated as associated with oxygen saturation in studies with COPD patients include reaction time and speed and coordination of simple motor tasks, problem solving and integration of perceptual and motor information – all abilities that would be expected to affect driving. Further research on the relationship of oxygen saturation in such illnesses to driving ability would be useful.

4.2.5 Central nervous system

4.2.5.1 Dementia

Estimates of frequency of dementing disorders, such as Alzheimers disease (AD) and Multi-infarct dementia (MID) vary from 5% of those over 65 (data cited in Johansson & Lundberg, 1997) to 15% of the same age group (Mortimer, 1983, cited in Kaszniak, 1991) rising to 47% probable AD in those aged 85 and older, an age group which is showing rapid population increase in Western nations (e.g. Evans et al., 1989). Dementia is defined as a progressive decline in cognition generally, but specifically affecting memory, reaction time, visuo-spatial skills, attention and problem solving, all abilities that would be expected to be central in maintaining safe driving, although in the early stages only one or two symptoms may be noticeable. Many older people with dementia, especially in the early stages, continue to drive, and many of these may be posing a considerable threat to themselves and to the general population. Carr's useful review (1997) cites two studies that find that 50% of AD patients had stopped driving by 3 years post-diagnosis (Friedland, Koss, Kumar, Gaine, Metzler, Haxby & Moore, 1988; Drachman & Swearer, 1993), implying that many patients continue driving for longer. Indeed, Friedland et al. found that for a group of AD patients who had had a car crash as drivers, the mean duration of their illness was four years (+/– 1.8 years). Carr's review suggests that risk of road accident increases with time since diagnosis.

Waller et al., (1993) noted that individuals with dementia had twice the crash frequency of non-demented age matched individuals, and Friedland et al. (1988) estimated an odds ratio of 7.9. Although this is a substantial increase in accident likelihood, Waller suggests that this crash risk is similar to that of normal healthy drivers under the age of 24 and is still substantially less than the crash risk of drivers who have been drinking alcohol (e.g., data from the first 2 to 3 years after diagnosis, Drachman & Swearer, 1993). In addition, some well-controlled studies have found no increase in crash incidence for drivers with dementia (Trobe, Waller, Cook-Flanagan & Teshima, 1996) or no significant increase in the early stages of this progressive disease (Drachman & Swearer, 1993). The results of Trobe et al. are surprising, since they did not separate out early AD patients from those who had received their diagnosis some time ago. However, they did find that their participants with a

diagnosis of dementia had a lower annual mileage, suggesting that such adaptations to driving were successful in reducing risk. Importantly, they found that patients with poorer scores on neuropsychological tests actually had lower crash risk than more mildly impaired AD drivers, and suggested that this may be due to reduced mileage and greater restrictions among the more severely impaired drivers. Stutts, (1998 – cited in Withaar et al., 2000) also found similar effects, such that drivers with cognitive impairments reported lower annual mileage and greater avoidance of high-risk situations. Evidence for the effectiveness of specific restrictions is rare in the literature, but the specific symptoms of dementia suggest useful restrictions that could be applied, and this is a field for further research. For example, symptoms of dementia such as impaired spatial awareness and processing suggest that drivers should stick to known routes; difficulties in reacting and making decisions quickly suggest that drivers should avoid busy times and places and situations where traffic is moving very quickly, such as motorway driving, or situations in which many sources of information have to be monitored, such as complex intersections. One striking piece of evidence for the usefulness of one adaptation comes from Bédard, Molloy and Lever (1996 – cited in O'Neill, 1996) who found that drivers with dementia who usually drove alone had a higher crash risk than those who drove accompanied.

As with other diseases reviewed here, an important approach is to examine actual function of patients rather than to make assumptions based on a diagnosis. Rather than using crash risk as an end measure of competence, as in the above epidemiological studies, some studies have taken a prospective, experimental approach and examined driving performance on the road or in simulators. These have shown that Alzheimer's disease (AD) patients generally perform worse than age matched controls (e.g. Bylsma, Rebok & Keyl, 1990), even when only mildly demented patients are selected for study (Fitten, Perryman, Wilkinson et al., 1995), although Hunt, Murphy, Carr, et al., (1997) report that even so, 55% of patients with mild or very mild dementia still showed safe driving skills on their particular on-road driving test (78% of healthy age-matched controls). Another approach is to examine laboratory measures in terms of their accuracy in predicting driving performance prospectively, or crash risk retrospectively (for a review, see Withaar, Brouwer & van Zomeran, 2000). Ball (1997) comments that in the early stages of the disease, performance on specific functional measures may be more likely to identify driving risk than does the general diagnosis. Measures that can be conducted in a clinic that can reliably predict which patients are not fit to drive would be a useful first screening device. One test that is widely available and widely used as a brief cognitive screening device in geriatric clinics is the Mini-Mental State Examination (MMSE – Folstein, Folstein & McHugh, 1975). Reports vary as to whether this test discriminates those who demonstrate adequate driving ability from those who do not, although the more recent and careful studies of Rebok et al., 1994 and Fitten et al. 1995, which have used on-road or simulator performance as measures (as opposed to reports of unsafe driving from relatives – (e.g., O'Neill, 1992; Lucas-Blaustein et al., 1988, cited in Withaar et al., 2000) find that it is a usefully predictive screening device, more so when scores are particularly low (Fitten et al.); see also other studies reviewed by Withaar et al., (2000). Importantly, results suggest that a high score on the test does not mean that a person is necessarily fit to drive, but a low score on the test (e.g., below 25 – Johansson, Bronge, Lundberg et al., 1996) would indicate that the person is probably not fit to drive. Tests of daily self-care and independence such as Activities of

Daily Living scales have also been shown by some authors to discriminate between drivers with dementia who show adequate driving ability and those who do not (e.g., O'Neill et al., 1992, cited in Withaar et al., 2000)).

Other more complex tests and batteries of tests have been examined in relation to on-road performance and accident history. Measures of visual attention is one group of tests that have shown promising results in terms of distinguishing between early/mild AD patients who drive safely in tests, and those who do not. Examples of such studies are those by Duchek, Hunt, Ball, Buckles & Morris (1998) and Ball, Owsley, Sloane, Roenker & Bruni (1993). Duchek et al. showed specific relationships between impaired driving and measures of selective attention, particularly in the ability to select relevant targets for attention and inhibit irrelevant distractors in visual search tasks. Ball et al. showed that a composite measure of visual attention, the useful field of view (UFOV) predicted crash frequency for participants with both good and poor mental status, and that individuals with poor mental status who did not have poor visual attention on this measure did not have increased crash risk relative to individuals with good mental status who also had unimpaired visual attention. Although Ball et al.'s group with poor mental status were a mixed group, not all of whom had a diagnosis of dementia, this study illustrates that variability within any group of mild AD patients needs always to be borne in mind. Studies that find significant differences in driving ability or visual attention between groups of mildly demented patients and controls (e.g, Rizzo, Anderson, Dawson, Myers & Ball, 2000) may be missing the important point that some patients within their dementing group may have good visual attention or be fit to drive while others most certainly are not. Other studies have shown clearly, although sometimes with a rather small number of patients, that variability in UFOV is greater for dementia sufferers than for normal age matched controls (Duchek et al., 1998). UFOV has been reliably related to driving performance and to accident likelihood in older drivers generally and in AD patients (see Ball, 1997; Ball et al., 1993) and these and other authors have suggested that this measure of visual attention is a better predictor of crashes than measures of general mental status.

Actual on-road driving tests are a vital part of any thorough screening for fitness to drive, especially where retraining is required or medical decisions based on diagnosis of dementia are being disputed. Dobbs (1997) examined the errors made by cognitively impaired drivers and compared them with those made by normal experienced drivers (both age matched and younger experienced control drivers were assessed). The analysis produced three categories of errors, one of which was made almost exclusively by the dementia patients, and which the author labelled as 'Hazardous or potentially catastrophic' because they could have resulted in a crash if the driving instructor conducting the test had not taken control of the vehicle or if the other traffic had not made avoiding responses. A second category of errors, positioning and observational errors, was made by all three groups of driving, although AD drivers made more than normal older drivers, who made more than younger experienced drivers. The final set of errors were errors which could all have resulted in a fail on a driving test, but which are not necessarily indicative of impairment in driving, such as speed errors or 'rolled stops'. These errors were made equally by all three groups, and the author suggested that they would not be useful to discriminate fitness to drive in older experienced drivers.

Finally, several medications have recently become available for mild dementia (the cholinesterase inhibitors). No specific data is available on their consequences for driving, but the resulting improvement in cognition could, in theory, prolong the time for which such a patient may drive safely. Regular in-depth review would be necessary for patients taking such medication. A further compound, memantine, has just been introduced for moderate-severe dementia but this indication suggests that these patients would already be unfit to drive. Specific research on the effects of the cholinesterase inhibitors on driving related function would be welcome.

Overview

There are many studies that demonstrate that dementia sufferers as a group have increased crash rate or poorer driving abilities as compared with age-matched controls. However, epidemiological evidence suggests that in actual case, risk is reduced by use of restricted driving practices. Trobe et al.'s data (above) suggest that reduced mileage or specific restrictions may be useful in reducing risk even in early stages of the disease. In the later stages of dementia, impairment is more global and severe and such adaptive restrictions may not be used as carefully, and there is little disagreement that driving is a serious risk (Lundberg, Johansson, Ball et al., 1997), the majority of patients giving up driving once impairment is severe. Most studies which examine variability find that many patients with very mild or mild dementia still drive safely, and specific screening devices which may help distinguish safe from unsafe drivers within this group are needed. Measures of visual selective attention seem the most promising potential tests, based on evidence of relationships with driving performance and crash risk, and some, such as the UFOV® are available to purchase, and other tests of visual selective attention are available or simple to construct. Thus, in the early stages it is discriminatory to prevent a person from driving without assessing their actual functional capabilities. It is suggested that 'a patient able to cope with day to day needs, retaining adequate insight and judgment, and not disoriented in time and space may be fit to drive' (Taylor, 1995; p101).

4.2.5.2 Parkinson's disease

Parkinson's disease (PD) is a progressive, age-associated neurological syndrome. Onset below the age of 40 is rare, with average age of onset in one survey being at 68 years (Kessler, 1972, cited in Kaszniak, 1986). In addition to the most obvious symptom of resting tremor, patients suffer from a general reduction in passive movement (rigidity), akinesia (impaired ability to initiate movements – the often seen 'freezing') and impaired postural reflexes (see Kaszniak, 1986). In early stages, the patient finds that movements are slowed and there is a loss of motor dexterity (e.g., it takes longer to get dressed), but in later stages movement control is severely affected to the extent that the patient may become unable to walk. PD is associated with depression and dementia at rates much higher than age-related norms, for example, estimates of the prevalence of dementia cited by Kaszniak (1986) range from 30 to 80%, with incidence seemingly related to stage of disease progression.

Both the movement and cognitive effects have potentially important implications for the PD patient as a driver. In particular, laboratory and simulator studies have found impaired steering accuracy, reaction times and interpretation of traffic signals in PD patients in the early stages of their disease (Madeley, Hulley, Wildgust et al., 1990 – cited in Poser, 1993) and that the extent of difficulties on a simulator correlated well with measured severity of PD on Webster's scale. Studies reviewed elsewhere in this document which have examined a variety of illnesses in relation to actual driving accidents in older groups, such as that by Koepsell et al. and Foley et al. have not included PD in their list of chronic diseases, and studies examining actual driving accident histories of PD patients are not numerous. One that examines this in self-reports (as opposed to using objective police records, for example) is that by Dubinsky, Gray, Husted, et al., (1991). They found that although PD patients had not, as a group, had any more accidents than controls, there was a smaller proportion of more severely disabled PD patients still driving – many had given up – and there were significantly more accidents in more severely disabled patients who did still drive. However, many studies find that most people with more severe PD give up driving, with the result that there are few drivers with more than mild PD to study. For example, Borromei, Caramelli, Chieregatti et al., (1999) found that only a quarter of the 204 PD patients in their study still drove, and they largely drove only short distances.

One particular area of concern in the literature relating to PD patients as drivers is the occurrence of excessive sleepiness that is common in this disease. Recent studies (Frucht, 2002 – cited in Progress in Neurology and Psychiatry, Digest) found that this was prevalent even in a study group in which patients suffering from dementia and cognitive impairments and severe symptoms were excluded. In this study, excessive daytime sleepiness was prevalent in 51% of study participants, the excessive sleepiness measure (Epworth Sleepiness Scale) correlating with severity and duration of PD and risk of falling asleep at the wheel (self-reports). 12% of these patients reported dozing while driving. None of these measures were related to any particular type of medication, although all study participants were taking various anti-Parkinson medications. The authors emphasised that actually falling asleep at the wheel was still a rare occurrence, and suggested that patients should be taught to recognise warning signs of drowsiness while driving. In another study that addressed the issue of whether the excessive sleepiness associated with PD is a function of medication or the disease itself, 25 PD patients who had never been treated with anti-Parkinson (dopaminergic) drugs were compared with treated PD patients and age and gender matched healthy controls (Fabbrini, Barbanti, Aurilia et al., 2002). Although there are issues as to differences in severity and duration of disease between the 'de novo' patients and those already taking medication, the findings indicate that sleepiness was significantly higher in the treated group. This does not unequivocally indicate that sleepiness is only related to medication, but does indicate that sleepiness may not be a significant problem in early, pre-treatment, developing PD.

Overview

As vehicle control is likely to be affected in this disorder, patients do need to report their condition to the DVLC, but it is recognised that many patients will be assessed as still capable of driving. As in other chronic diseases, level of function is a more important criterion than diagnosis itself. However, few PD patients find themselves able to continue driving once their disease has progressed beyond early stages.

4.2.5.3 Psychiatric illness

Chick (1995), in Taylor's *Medical Aspects of Fitness to Drive* document, reports that psychiatric illness slightly increases the risk that a driver will be involved in a road traffic accident (RTA) and that this increase is mostly accounted for by anxiety, dementia, depression and alcoholism. Psychotic illness has generally not been associated with increased accident rate, but serious personality disorders has. Suicidal intent is sometimes implicated in a crash (see below). Most studies examining the association of psychiatric illnesses with driving have not been conducted with older drivers, and a useful review is that by Silverstone (1988). In summary, Silverstone cites several studies in which small and selected groups of patients or accident involved drivers are assessed: A retrospective study by Selzer et al., (1968) found that 22 of a group of 96 drivers who had been killed or injured in road accidents as drivers were described as 'Paranoid' by the authors, having interviewed significant others or surviving drivers, compared with 4 controls; a further 20 were depressed (7 controls) and 9 of these were suicidal (1 control). Crancer and Quiring (1969) compared 271 psychiatric patients with norms for the rest of the population of the same county, and found that the accident rate for the patient group was twice that of the control group, but that there were considerable differences between diagnostic groups, with schizophrenia being notable for lack of increase in road accident rate. Finally Silverstone describes a study by Kastrup, Dupont, Bille, and Lund (1978) who conducted a larger scale and better-controlled study in Denmark where all RTAs are filed centrally, as are all admissions to psychiatric in-patient units. They identified all psychiatric inpatients over a two-year period who had been involved in a RTA where at least one person was injured. Overall, male patient drivers accounted for 4% of all RTAs in Denmark, women patients for 6.5%, and since psychiatric admissions during the course of the 2 year period involved less than 1% of the population, the contribution to RTAs is very disproportionate. Again, there was a large difference in involvement between diagnostic groups, these authors again finding that a diagnosis of schizophrenia was not associated with an increase in RTAs.

More recently, Vernon, Diller, Cook, Reading, Suruda and Dean (2002) found that drivers declaring 'psychiatric' conditions on their driving licence in a large scale study (6,808 drivers declaring psychiatric illness, 6,481 of whom had no consequent licence restrictions) in Utah, U.S.A., had a significantly increased relative risk of having a crash (relative to age matched control drivers).

See Section 5 for a discussion of the effects of commonly prescribed medication in psychiatric conditions.

(i) Schizophrenia

In both the Kastrup et al. study and the Crancer and Quiring study (Denmark and US respectively, cited in Silverstone, 1988), patients suffering from schizophrenia were not found to have an increased RTA rate.

(ii) Bipolar affective disorder

Despite disinhibited and reckless behaviour in the manic phase, there is no reliable evidence to point towards increased RTAs.

(iii) Depression

Traditionally, incidence of depression is expected to rise with old age given increases in bereavements, possible loneliness and ill health. The prevalence of treated depression among community dwelling older people is estimated as 5%, with an estimate of 15% for all depression, including that not diagnosed or treated (Blazer, Hughes & George, 1987). Blazer (1989) suggests that with the increase in depression among younger people, the traditional finding of a higher incidence of depression among older people may be diminishing, although suicide among older men in particular is still high. Depression results in effects such as slowing of response, poor attention and judgment, and occasionally confusion, but in older people these add to existing effects of age on, for example, speed of information processing or reaction time. However, evidence finding a relationship between depression and accident risk or driving performance is not conclusive. For example, Margolis, Kerani, McGovern et al., (2002) found no relationship between depression as measured on the Geriatric Depression Scale and accident risk for a large group of older women drivers, although numbers in the study with depression were low, and Sims, Owsley, Allman, Ball & Smoot (1998) found no significant difference in incidence of depression between a group of older people who had had a crash and those who had not. In contrast, Foley et al., (1995) found a significant increase in relative risk of crash incidence for those patients in the highest fifth of depressive symptoms among their large sample, but the increase in relative risk associated with taking antidepressants was not quite statistically significant, although the contributions of each to increased risk in the other were not controlled for statistically. Koepsell, Wolf, McCloskey, et al. (1994) found that a diagnosis of depression was associated with a marginally significant increase in risk of a traffic accident, and Hu, Trumble, Foley, Eberhard & Wallace (1998) found a highly significant association between taking antidepressants and crash risk for older male drivers, but not for older female drivers. While a study separating out the effects of symptoms and medications would be extremely useful, these studies suggest at least some relationship, with differences between mildly and more severely affected patients and also between men and women, which may be obscuring some findings.

In addition to the cognitive effects of depression and of antidepressive medications (see section 5), depressed drivers may also be suicidal and this may cause them to crash their car in an attempt to end their lives. For example, Schmidt et al. (1977 – cited in Silverstone, 1988) analysed the adjustment profiles of 182 drivers involved in fatal RTA and 96 involved in non-fatal RTA. They concluded that in only 1.7% of the fatal RTAs was there probable suicidal intent (this rose to 2.7% when single vehicle accidents only were considered).

However, Silverstone's analysis of Isherwood et al.'s (1982) data noted that 10% of 100 hospitalised RTA drivers appeared to be suicidal or possible suicidal. A detailed study, spanning nearly 20 years, was conducted by Hernetkoski and Keskinen (1998) in Finland, a country with a particularly high suicide rate. These researchers found that the percentage of fatal accidents that could be carefully classified as suicides rose during the period studied from 1.1% in 1974-75 to 7.4% in 1991-92. Suicide drivers were significantly older than drivers dying in accidents attributed to negligence, and although the majority were aged 25-34, drivers over the age of 55 made up approximately 8% of the suicides (fig. 2, p702).

(iv)   Anxiety

Actual driving studies with patients suffering from anxiety are rare, but laboratory studies show impairment of psychomotor function. Crancer and Quiring (1969 – cited in Silverstone, 1988) found that patients with psychoneurotic disorders had 50% more accidents than controls – but anxiolytic drugs such as diazepam also increase the risk of RTAs (see below, Section 5: Skegg et al., 1979, Honkanen et al., 1980). The question remains as to whether the risk is greater from the anxiety or from the drugs? Stress and anxiety does cause an increase in RTA risk. In a study of drivers involved in fatal RTAs, drivers were much more likely to have had a serious quarrel in the last 6 hours before their accident than control subjects (Selzer et al., 1968, cited in Silverstone). Although in studies, life events and subjective stress rating have been correlated with accident risk, it seems to be a very small relationship. For example, other work has found no such significant relationship (Isherwood, Adam and Hornblow, 1982 – cited in Tsuang, Boor & Fleming, 1985) – so perhaps the risk related to the drugs is greater.

(v)   Personality disorders

Personality disorders probably account for more accidents than any other mental and physical disorders combined: behaviour resulting from aggressiveness, impulsiveness, intolerance of others and driving regardless of significant alcohol consumption all result in seriously increased risk. The greatest increase in RTA risk is seen for male patients with personality disorder, especially of an aggressive or belligerent nature. Silverstone's (1988) review indicates an increase in accidents for such patients. For example, he cites Eelkema et al. (1970) who found that male patients with personality disorders had 6 times as many RTAs as controls, and Kastrup et al., (1978) who found that those patients diagnosed as 'personality disorder' were involved in a disproportionate number of RTAs. Studies examining such disorders specifically in older drivers were not found.

(vi)   Alcoholism and other substance abuse

This area is by far the most important in the RTAs attributed to psychiatric patients – especially alcohol abuse – those whose drinking is described as out of control. However, alcoholism is generally not thought to be a big issue for older drivers as alcohol related RTAs more often involve younger drivers. For example, Rehm and Ross (1995) found a statistically significant lower rate of alcohol intoxication among older drivers who had been involved in an accident as compared with drivers aged 40 to 59. However, alcoholism is thought to be grossly underestimated as a problem in

older people, with one American study finding a positive identification of alcoholism in 21% of new admissions to hospital aged over 60 (compared with 27% aged under 60) (see Caracci & Miller, 1991, for a review). Alcoholism is more common in older men than women, and widowers over the age of 75 have the highest risk of alcoholism of any group (Glass et al., 1995, cited in Hoyer, Rybash & Roodin, 1999). Dupree and Schonfield (1996 – cited in Hoyer et al.) report that older women seem to be at higher risk of abuse of prescription medications. However, studies examining relationships of alcoholism or substance abuse with accident risk specifically in older drivers were not found.

Overview

Although studies specifically examining the effects of psychiatric illnesses on road safety in older drivers were not found, it is suggested that psychiatric illnesses that affect cognitive factors such as speed of processing or attention, notably depression and anxiety, may exacerbate existing age-related changes in cognition and reduce the reserve cognitive capacity available to compensate for such effects, increasing risk. Suicidal intent in the accidents of depressed older drivers is not unknown.

4.2.5.4 Other neurological disorders

(i)   *Vertigo or dizziness*
Vertigo is an impairment of the vestibular system resulting in balance difficulties and dizziness, which increases in frequency with old age. While a major concern for such sufferers is falls, Poser (1993) suggested that attacks may cause a patient to lose control of a vehicle and that driving should be avoided until attacks have ceased.

(ii) *Syncope* (loss of consciousness, fainting)
Syncope, or fainting, is associated with several disease processes, for example, hypotension, ventricular arrhythmias and, perhaps most commonly (Sheldon and Koshman, 1995), neurological origin.

Rehm and Ross (1995) reported that 12 out of 84 drivers aged over 59 involved in injury accidents had had definite syncopal episodes leading to their crashes. Koepsell et al., (1994) included syncope in their analysis of medical conditions and older drivers and did not find a significantly increased relative risk of accident for this group, although did note that this condition was rare in their group. Sheldon and Koshman (1995) describe studies that have shown that up to 75% of syncope is neuromediated, using 'head-up tilt table' testing of patients. Out of their group of 209 patients (all of whom were drivers) with a history of untreated neuromediated syncope, only 5 had a history of fainting while driving, resulting in accidents. For patients with a positive 'tilt-table' test who had experienced at least one syncopal episode, the authors calculated the risk of fainting while driving as 0.33%/driver year, and the risk of the faint causing an accident as 0.26%/driver year. However, although the authors reported that only 7 people who had experienced such a syncopal episode had given up driving, data were not presented on the extent of driving still undertaken by these patients. As noted in Section 4.1 above, many patients who are aware that their condition

would be expected to increase driving risk may not necessarily give up driving, but may reduce or restrict driving in specific ways. In addition, the authors do not present data on the extent of presyncopal warning symptoms, or prodrome, in their studied patients. They also do not compare accident risk with a control group to determine relative risk, which would be a useful further analysis to do in future research. They do suggest that patients without reliable presyncopal prodrome, should not drive, and that patients presenting with frequent episodes or with their first syncopal episode should be advised not to drive at least for 3 months, resumption of driving depending on outcome of treatment and occurrence of further episodes. Nevertheless, the authors suggest that risk of accident is very low for patients with reliable and prolonged prodrome and that most such patients should be allowed to drive.

(iii) Epilepsy

Bearing in mind that drivers with uncontrolled risk of a seizure are not allowed to drive in the UK, drivers with epilepsy have still been generally found to have an increased crash risk, with one source putting this at almost twice the risk of other drivers (e.g, Waller, 1965). For example, in Taylor's (1983) study of 2000 acute collapses at the wheel while driving and leading to police reported accidents involving personal injury, over 50% of cases, were associated with epileptic seizures. Thus, although a large proportion (approximately 70%) of epilepsy sufferers can have their seizures adequately controlled by means of medication, these patients still seem to be at increased risk of serious injury on the roads, although the medication clearly reduces risk. However, some anti-convulsants do result in cognitive impairment (e.g. phenytoin), although others are less likely to (e.g. carbamazepine, see section 5.17)

Other studies have found that epilepsy patients who do drive seem to have about average accident rate, but with a greater injury and fatality involvement. Chadwick and Taylor (1995, unpublished, cited in Chadwick, 1995) examined this accident rate by questionnaire of 17,000 British drivers declaring epilepsy to the licensing authority and comparing it with 8,000 randomly selected drivers. Drivers with epilepsy had about the same overall road traffic accident involvement as controls, but with more casualties requiring hospital admission beyond 24 hours. Drivers with epilepsy also had greater involvement in fatal road traffic accidents. Greater risk of accident (all crashes and also at-fault crashes) compared with age-matched controls was found in Vernon, Diller, Cook et al., (2002), but notably, a greater risk of citation for traffic offence was not found for drivers declaring epilepsy on their licence. Studies examining epilepsy specifically in older drivers are uncommon, comparatively, and some otherwise thorough examinations of the relationships of illnesses to driving in the older group, such as that by Foley et al. (1995, see above) do not include it. Hansotia and Broste (1991 – cited in Koepsell et al., 1994) found little difference between the relative risk of accident for epilepsy sufferers of all ages (1.33) and that for epilepsy sufferers aged over 65 (1.39).

(iv) Excessive sleepiness

Horne (1992) reported that daytime sleepiness may have been responsible for 20% of accidents on a British motorway in a police survey. Data from the USA national highway transportation safety administrations Road Traffic Accident statistics for 1990 indicated that daytime sleepiness was a major factor responsible for 1% of the total of 57,000 crash reports. 96% involved a passenger vehicle. 77% were male drivers and the peak time of crash was between midnight and dawn, and most involved a single vehicle. Causes of excessive sleepiness are most commonly secondary to fatigue, persistent insomnia, shiftwork, burning the candle at both ends, drugs (see below) and alcohol. Even a short sleep loss for one hour each night for a prolonged period has a cumulative effect on wake time performance (Parkes, 1995). Primary causes of excessive sleepiness are symptomatic sleep apnoea – (see above) and Narcoleptic syndrome. This is a lifetime, neurologically based, illness with a prevalence of 5 per 10,000. Incidences of causes of excessive sleepiness such as persistent insomnia and sleep apnoea significantly increase with age.

The period of low vigilance in circadian rhythms is between 1400-1700 hours and in those awake at night between 0200-0700. These normal vigilance changes are exaggerated in persons with excessive sleepiness. However, laboratory studies of cognitive performance have shown important differences in cyclical variability between young and older people, with younger people showing better performance later in the day, but older people showing better performance in the morning, deteriorating towards evening, with evidence showing specific exacerbation of age-related deficits in attention and ability to inhibit distracting information (see Yoon, May and Hasher, 2000, for a discussion of this field).

Overview

A key point to bring out in relation to the neurological disorders discussed in this section is that although the frequency of these illnesses may increase with age, and some such illnesses do have effects on driving safety, there is not sufficient evidence here to suggest that the influence of such illnesses on driving is any greater for older drivers than the same illness in a younger person. However, specific research comparing different age groups is rare.

4.2.6 Endocrine system

4.2.6.1 Diabetes Mellitus

Incidence of diabetes becomes much more common with increasing age, with 17-20% of 70 year olds having difficulty regulating glucose (as compared with 1.5% of 20 year olds: Sullivan, 1986). In Taylor's 1983 study of 2,000 acute collapses at the wheel while driving and leading to police reported accidents involving personal injury, 17% were associated with hypoglycaemia in persons with insulin dependent diabetes. Earlier reports noted that crash experience is approximately twice that of other drivers (Crancer and McMurray, 1968; Waller, 1965) but more recent research, (Hansotia and Broste, 1991 – cited in Hansotia, 1993) found a more modest increase in crash risk for a representative sample. Hansotia and Broste noted that with improved medications, better monitoring by diabetic patients of their

own blood glucose levels and improved understanding of diabetic control, the estimated 'mishap ratio' or crash risk factor is now 1.32 – less than previous estimates of about 2. However, with more current tighter control of blood glucose levels, clinically obvious hypoglycaemic episodes are much more common. Also, important cognitive changes often occur with only modest levels of hypoglycaemia at times when individuals may be totally unaware they are hypoglycaemic (Hansotia, 1993).

Studies examining older drivers specifically are less common, but Koepsell, Wolf, McCloskey et al., (1994) found an increased relative risk of accident for older drivers suffering from diabetes mellitus of 2.6, and then examined diabetes in more detail in terms of specific features of diabetes, for example, treatment, length of duration of illness and co-existence of heart disease. There was no evidence of increased risk of accident among those patients who were treated by diet alone, with a three-fold increase of relative risk for those treated by oral hypoglycaemics and almost a six-fold increase for those treated with insulin. Those most at risk were patients who also suffered from heart disease, and risk increased with increasing duration of the disease. Notably, these researchers found that the highest increase in risk of accident among a variety of chronic diseases was that for diabetes, and suggested that the transient impairments of cognition that accompany more serious diabetes (drug treated) were primarily responsible. Other studies have not found an association between crash risk and diabetes, but these tend to be studies with few diabetic patients, who have not separated out patients into treatment groups (e.g., Sims, Owsley, Allman et al., 1998). Koepsell et al.'s results would suggest that any group of diabetic patients that are not predominately serious enough to be treated by oral hypoglycaemics or insulin would not show an association with crash risk. Hansotia and Broste's (1991) overall 'mishap ratio' was lower than that reported by Koepsell et al., as would be expected when risk is calculated for the group as a whole, rather than separated into groups according to treatment or duration of illness, but they notably demonstrated no increase in the relationship of the illness with crash risk with older age – the ratio for diabetics over the age of 65 was 1.39, not significantly different from that for the group as a whole (1.32), although the risk for diabetics under the age of 25 was lower than that for other groups (cited in Hansotia, 1993). One study which attempted to examine crash risk specifically in older diabetics, and which also examined risk as related to treatment group is that by McGwin, Sims, Pulley and Roseman (1999). This study investigated older drivers who had experienced a crash and carefully controlled for a variety of factors, including other disease processes. They found no association between diabetes and crash risk except for older diabetics who had experienced another crash in the preceding four years. Diabetic drivers were more than twice as likely to have been involved in another accident as the control group. These authors also found no increase in crash risk with increase in severity, as indicated by treatment type. Thus these results indicate that although increase in crash risk may not be universal among diabetics, there are some diabetic drivers who clearly do seem to become more accident-prone. Although these authors adjusted their analyses for age, they did not present the extent to which age contributed to the analysis, which would have been a useful addition.

One of the most important criteria for safe driving is that a patient is able to recognise the signs of hypoglycaemia, and in some patients with diabetes of long duration, diabetic autonomic neuropathy develops and they may lose their ability to recognise hypoglycaemia. In addition, Hansotia (1993) recommends that those taking beta-adrenergic blocking agents should also be counselled to take precautions as such drugs can interfere with recognition of hypoglycaemia.

If diabetes is treated other than by diet alone, sufferers must report their condition to the DVLA by law. Group 1 drivers (i.e. private drivers) treated with insulin must demonstrate satisfactory control, recognise warning signs of hypoglycaemia and also not suffer from a relevant disability. Diabetic patients on insulin are barred from applying for an LGV or PCV driving licence and from renewing such. Patients who lose their ability to recognise warning signs of hypoglycaemia are not allowed to drive.

Overview

Studies specifically with older drivers have indicated that serious diabetes (treated with oral drugs or with insulin, as opposed to being treated by diet alone) is one of the strongest predictors of accident as a driver, showing a stronger relationship than other illnesses examined. Studies that have shown only a moderate increase in risk have generally not separated out participants into treatment groups. Other studies have shown that some diabetic drivers do seem to be at particularly high risk of multiple accidents. Although there are findings of increased risk with increasing duration of disease, there does not seem to be a reliable, separate increase in risk with increasing age of diabetic over and above any increase in risk associated with age itself.

4.2.7 Musculo-skeletal and joint diseases

4.2.7.1 Arthritis

The term 'arthritis' covers a group of disease processes affecting the joints. Among the most common are rheumatoid and osteoarthritis. Rheumatoid arthritis is not necessarily age related in onset, but by its nature as a progressive disease, its effects become more debilitating with increasing age. Osteoarthritis is age related and shows an exponential increase in occurrence over the age of 50, such that some form of arthritic degeneration in joints is believed to be present in all people aged over 70 (Tonna, 1986). Women seem to be at higher risk of both types of arthritis than are men (Roberts & Roberts, 1993, Tonna, 1986).

The physical difficulties of driving with substantial joint degeneration are the prime concern of older drivers with arthritis, although the many vehicle adaptations available go some way towards enabling patients to continue driving for longer. Adaptations to steering, braking and acceleration controls are available, as are special mirrors to increase visibility when head turning, especially to the rear, becomes difficult. Referral to DVLA disabled drivers assessment centres is often useful (a list can be found in Medical Aspects of Fitness to Drive, 1995). Roberts and Roberts (1993) divide the physical effects of arthritis on driving into two main factors, the effect of pain producing involuntary hesitancy of movement, and

the absolute restriction of range of movement. These authors cite a study by Cornwell (1987) who found that muscle strength differences between people with and without osteoarthritis were no more in magnitude than the normal gender differences found in the same measures, and suggested that pain and movement restriction were of much more importance in restricting driving than any decline in muscle strength. In the more debilitating rheumatoid arthritis, strength declines are greater, but, Roberts and Roberts assert, this is still not enough to prevent safe driving, given the availability of power-assisted steering.

However, arguably of at least equal concern are the cognitive effects of the various medications taken, and NSAIDs have been highlighted in studies as being related to increased accidents. Importantly, McGwin et al. (2000) have shown that the contributions of the illness itself and of NSAIDs prescribed are independent predictors of accident risk (see Section 5).

5 Effects of medication on driving-related abilities

There have been many studies relating to the effects of medication on driving ability, and these have been summarised in several reports. Some of these reports include risk estimates for individual substances (Maes et al., 1999; Gemmel et al., 1999; and prescribing guidelines (Alvarez et al., 2001). The British Medical Association has recently published a major resource document on driving under the influence of drugs (BMA, 2002). The DTLR has also produced a report on over-the counter (OTC) medications and their potential for unwanted sleepiness in drivers (Horne & Barrett, (DLTR, 2001). From these evaluations, it is clear that there is an excellent consensus on a variety of medications, especially psychoactive agents, that present a risk to all drivers, including anxiolytics/hypnotics (especially of the benzodiazepine group), tricyclic and 'second generation' antidepressants, centrally acting analgesics and first generation antihistamines. However, few studies, and even fewer reviews and reports, have considered the particular risks that medications may pose for the older driver. Those that have, have generally considered groups of medications or general relationships between taking any prescribed medicine at all and having an accident. However, as noted in the introduction, in many of the studies reviewed we do not know whether the medicine being taken is the cause of any increased risk, or the illness that results in the medicine being necessary, the medicine itself possibly reducing the risk of the ill person.

Older people are more likely to be taking medication than their younger counterparts. Older traffic-accident victims are more likely to have been taking 'traffic-dangerous drugs' than younger people similarly involved, regardless of whether there is any question of fault on the part of the victim (Everest, Tunbridge & Widdup, 1989; Johansson, Bryding, Dahl, Holmgren, et al., 1997). In addition, within the 'elderly' group, the incidence of such medications in road accident victims has been shown to increase further with advancing age (Everest et al., 1989; Johansson et al., 1997).

It is often of more consequence whether a person makes dangerous decisions (e.g., drivers under the influence of alcohol have been shown to attempt gaps that are far too small, but their actual ability to negotiate safe gaps in terms of motor coordination is not altered) or whether they have perceived important information. The emphasis in much of the literature is on the ability to negotiate normal traffic rather than the ability to cope with unexpected situations. Walsh (1984) noted that many drugs may only impair well-learned behaviour at high doses, but at much lower doses they may impair coping or learning skills, for example, route finding on what to do if someone runs out in front of the car.

In making the decision to prescribe a medication that may affect driving-related abilities, it is important to take into account a patient's overall health requirements, including the impact on lifestyle of advising against driving. To what extent the possible effect of a particular medication on driving can be taken into account will vary according to the nature and severity of the disorder it is being prescribed for, as well as the availability of alternative treatments. In evaluating the possible impact of a medication on driving, it is important to remember that medication is prescribed for an illness, and that the illness may itself affect driving-related abilities. A particular medication could affect driving

independently, it could worsen any deterioration in driving ability caused by the illness, or it could even act to reduce the risk to the patient caused by the illness. Examples of each of these interactions will be found in the ensuing sections.

Finally, there are complex problems due to the vast number of different drugs in any one category, which vary in their effects and side effects, combined with the fact that different people may react in different ways to individual agents.

5.1 Investigation of drug effects on driving-related abilities

Two major approaches have been taken to the study of drug effects on driving-related abilities, the experimental and the epidemiological. Each has advantages and disadvantages. Experimental studies allow the effects of the medication to be investigated independently of the illness, because the subjects to be included and the experimental design are chosen by the researcher. In contrast, epidemiological studies examine the real-life impact of medication on crash-risk, but by their nature it is difficult to disentangle this from the impact of the illness for which the medication was prescribed.

5.1.1 Experimental studies

In experimental studies, a medication (or placebo) is administered to the chosen sample of patients or healthy volunteers and the effects on driving, or driving-related abilities, is examined. A major advantage of these studies is the degree of control that can be exerted over potentially interfering variables, and the rigour of the experimental designs (including blinding, crossover and randomisation) that can be applied. Studies of this type are essential to dissect out individual contributions of the medication and the disorder, to driving-related deficits.

(i)   Neuropsychological test batteries have been used extensively in predicting the effects of medication on driving ability. Such batteries may contain tests that measure short-term and delayed recall, attention and divided attention, psychomotor variables such as critical flicker-fusion threshold (CFF) and reaction time, especially choice-reaction time, among others. While these tests clearly measure relevant components, no single test or test battery has yet been shown to predict, adequately, the effects of these medications in real-life driving situations (O'Hanlon & Ramaekers, 1995). Tests of hypovigilance have failed to demonstrate significant results even in the presence of overt somnolence or impaired 'real' driving (Maes et al., 1999); suggested reasons for this may include assessment of only a limited number of cognitive functions, too short a test period to mimic sustained function and inability to detect disinhibition and increased risk-taking (Maes et al., 1999).

(ii)   Subjective awareness of impaired function, measured by visual analogue scales, has been included in many studies and has been repeatedly shown to be a poor indicator of the impairment recorded during actual driving tasks (Gengo & Manning, 1990; O'Hanlon & Ramaekers, 1995, Vermeeren et al., 2002). This is a major finding because it questions the adequacy of current UK warning label requirements.

(iii) Driving simulation: Objective data on drivers' actions in response to projected road situations can be obtained in driving simulators but the predictive validity of simulator tests has not been established (Ray et al., 1993). Maes et al., (1999) comment on the low motivational level of the volunteers due to the absence of personal risk.

(iv) 'On-road' driving: Certain European centres have sought to overcome these drawbacks by means of a 'real driving' test in a dual-control car (see O'Hanlon & Ramaekers, 1995). These studies generate high-quality objective data on car manoeuvring, such as the Standard Deviation of Lateral Position (SDLP), a test of the amount of weaving. Criticisms include that there is an 'important lack of risk evaluation studies' (Maes et al., 1999), in that reactions to unexpected situations are not covered. Also, there is an inevitable tendency for the driver to be on his (or her) 'best behaviour'.

While potentially valuable information may be gained from experimental studies, it is generally accepted that they cannot completely model 'free' driving. (Irving & Jones, 1992; Ray et al., 1993). In addition, these predictive studies are likely to differ from the 'real-life' situation with respect to medication: Most volunteer studies have concentrated on healthy younger adults using doses within the therapeutic range, which may not predict adequately the situation in special patient groups such as the elderly. Females may differ from males in their sensitivity to a medication. In general use, a finite proportion of the patients taking a medication may be more, or less sensitive to its effects and experimental studies are likely to exclude the top 5-10% of a population with respect to sensitivity to sedation (O'Hanlon & Ramaekers, 1995). Volunteer studies either employ single doses of a medication or its administration for a restricted period of time. In contrast, patients may be maintained on medication indefinitely and may be suffering from a variety of other disorders. Such co-morbidity and subsequent polypharmacy may adversely affect the pharmacokinetics and pharmacodynamics of individual items of medication. An additional contribution from non-prescribed, OTC medication should always be considered.

5.1.2 Epidemiologic studies of Road Traffic Accidents (RTAs)

Epidemiological studies are essential both to discover the impact of medication in the 'real-life' situation and to validate (or otherwise) the results of experimental tests. A major strength of epidemiological studies is the relevance of the outcomes (Ray et al., 1993).

The increasing availability of computerised databases has made possible the study of very large groups in 'pharmaco-epidemiological' surveys. In this type of study, a database of, say, police accident records or hospital treatment following a road traffic accident (RTA) is matched against a database of prescriptions dispensed. This is a very powerful technique (Maes et al., 1999) but, with rare exceptions, has so far only been able to detect class effects since, even with very large populations, searching for matches on two comparatively rare events (RTA and prescription of a particular drug) produces relatively small numbers. Neither concordance with a prescribed medication regimen nor concomitant use of OTC preparations can be controlled for using this method and, in some studies, the 'at fault' status of the proband is unknown. Also, drug effects may not be clearly distinguishable from

the consequences of the disorder they are being used to treat (Lemoine, 1996). Nevertheless, the information such studies can provide on the change in risk due to medication classes of interest is, arguably, the most valuable data currently available to guide prescribing.

Pharmaco-epidemiological investigations use two principal measures of risk: the Relative Risk (RR) is appropriate to cohort studies, where groups within the cohort are defined by the presence or absence of an occurrence, while the Odds Ratio (OR) is used for case-control studies and estimates the relative risk in the case group compared with a (matched) control group.

One question pharmaco-epidemiological studies cannot cover is whether the medication being considered was actually a factor in causing each individual RTA (Gemmell et al., 1999). Investigation of relationships between illness, medication and crashes is also difficult for statistical reasons. So far, only one study has attempted to systematically examine such interrelationships: the 'Alabama' study (McGwin et al., 2000) was able to look at the interactions between certain medication classes under study and the illnesses for which they were prescribed. However, in this report, data on medication and illness was based only on patient recall elicited through telephone interview and, as the authors state, statistical power was not high. Its findings will need confirmation before their reliability can be fully judged.

In more specific studies, most attention has been given to medications that act on the central nervous system to produce their therapeutic effects. However, direct CNS activity is not the only prerequisite for a medication to present problems. For example, poor glucose control in a diabetic, or development of hypotension during administration of an antihypertensive, could both compromise brain function. Ocular medications may affect vision and even an apparently innocuous form of treatment such as a diuretic could present sufficient discomfort to distract the driver. For these reasons, we have taken a systematic approach, based on the classification system employed by the British National Formulary (BNF).

Since 1994, the EU Committee for Proprietary and Medicinal Products guidelines state that package inserts must include a statement on a drug's effects on the ability to drive. In the UK, cautionary and advisory labels are required for dispensed as well as OTC medicines and the relevant warning labels are keyed to individual medicines in the BNF. These labels and package inserts are supplied at the point of dispensing and so the prescriber may be less aware of them. Nevertheless, they are all noted in the BNF, providing a useful aide-memoir to the need for further counselling. A list of the relevant warnings is given below. However, these warnings are directed mainly at substances causing drowsiness and, as such, do not offer a definitive guide to the range of substances that may pose problems for the older driver. Furthermore, as will become apparent in later sections, and noted in Section 4.2.4 in relation to sleep apnoea, perceived drowsiness can be a poor indicator of functional impairment and, for some of the substances to be discussed here, more restrictive instructions may be advisable.

This review will include only those medicines licensed (or believed to be near to licensing) for therapeutic use in the UK. Illegal substances will not be included. Many patients self-medicate with products, including herbal remedies, obtained OTC (DTLR 2002) and this

may compound the risk to driving when taken with prescribed medications. It is possible that this may be less of a problem in older patients, who do not pay a prescription charge in the UK, although self-reports from large-scale studies such as that conducted at the Age & Cognitive Performance Research Centre in Manchester suggest that older people do self-medicate, for example, with herbal remedies, vitamin supplements and OTC drugs to a large degree. Nevertheless, counselling on concurrent OTC medication should be given whenever an agent presenting a possible risk to driving is prescribed.

Cautionary and advisory labels for dispensed medicines (BNF)

Label No.

2:      Warning. May cause drowsiness. If affected do not drive or operate machinery. Avoid alcoholic drink.

3:      Warning. May cause drowsiness. If affected do not drive or operate machinery.

19:     Warning. Causes drowsiness, which may continue the next day. If affected do not drive or operate machinery. Avoid alcoholic drink.

5.2 A note on the effects of alcohol on older drivers

Although alcohol and driving is not the focus of this review, a brief note on the effects of alcohol on older drivers is presented here. Specific information on interaction of alcohol with various medications is presented in the following sections where appropriate.

Alcohol affects older people differently. Waller (1992) describes the differential effect of alcohol on older people:

(a) A given dose of alcohol results in a higher blood alcohol concentration (BAC) in an older person because of reduced water content of the blood as compared with a younger person of similar weight and sex.

(b) Older drivers have been shown to have a steeper climb in crash risk at BACs under 0.10g/dL than do middle-aged persons (Hyman, 1968), perhaps because alcohol can also increase night blindness and glare sensitivity, narrow visual search and alter contrast sensitivity, as does normal ageing. Also, a person driving with reduced reserve processing capacity due to age-related slowing in information processing will suffer greater obvious effects of alcohol because of the lack of 'spare' processing capacity.

(c) Hangover electrolyte and other neurological imbalances may persist longer and be more serious for older drinkers.

Importantly, given the increase in medication use among older people, interactions with alcohol are a greater risk.

In a careful study which excluded alcoholism, other chronic conditions and medications which may affect driving, Quillian, Cox, Kovatchev and Phillips (1999) examined the effects of age and alcohol on simulated driving (using men only). They found that although older men showed poorer driving on the simulator than middle-aged men on a number of measures, there were few statistically significant interactions between age and intoxication. One significant interaction was that older men braked inappropriately more often than middle-aged men when sober, and much more so when intoxicated. A finding of note was that although the majority of drivers in both age groups reported feeling intoxicated (all were legally intoxicated at BACs of approximately 80mg/dl, although they were not aware of their precise BACs), 79% of the older drivers said they would choose not to drive after having experienced simulator driving in their intoxicated state as compared with 43% of the middle-aged drivers, a significant difference, suggesting that the older people were generally acutely aware of their impaired driving. Importantly, although this study did not show a significantly greater effect of alcohol for the older drivers, it did demonstrate that older drivers were starting from a lower level of performance, from which an equivalent deterioration would bring them to a lower level of performance than it would for younger drivers starting from a higher level of performance.

5.3 Driving-related skills and the effects of medication

Driving is an over-learned and over-practised skill, yet dependent on transient external circumstances (Lemoine, 1996). The component skills that may be affected by medications (Gengo & Manning, 1990; Maes et al., 1999) have been suggested to include:

Perception: including visual acuity, attention (focus and scope), recognition, discrimination.

Anticipation: of the actions of oneself and of others, of the risks in prevailing road circumstances and in short-term memory.

Decision-making: on the basis of perception and anticipation, of what one can foresee and of prior experience, learning and knowledge. This attribute of driving includes states of mind that can be altered by medication such as risk evaluation, caution/impulsiveness as well as orientation in time and place and aspects of memory such as delayed recall. Reaction time should be included here, including execution of appropriate reactions in an emergency.

Action: Motor activities of car control based on all of the above, including both continuous and discrete actions. Psychomotor integration, fine motor skills, muscular coordination, muscle strength, postural control and, highly relevant to older drivers, possession of the necessary range of movement while sitting.

A central issue here is that of reserve capacity. A small decrement in cognitive resources may be easily accommodated in a person with plenty of reserve, but in a person operating nearer the edge of their capabilities, that small decrement may be devastating. This may be because they have reduced information processing resources, related, perhaps to old age, or because other problems of old age are already taxing their information processing resources to the limit, for example, a visual deficit that requires more effort to be expended in gathering needed information from the visual scene.

Attempts to predict the impact of a medication on driving ability have utilised two approaches: experimental and epidemiological.

5.4 Altered sensitivity to medication in older patients

A central issue in this document is that older patients are likely to exhibit altered sensitivity to medication (Moore & O'Keeffe, 1999), especially to their cognitive effects (Molchan et al., 1992; Zemishlany et al., 1991) and this should be taken into account when prescribing. This change is most often in the direction of an increased effect, including side effects and adverse reactions, and the duration of action of a drug may be significantly prolonged. The reasons for this are well understood and only a summary will be given here. For further reading, the succinct series of articles by McGavock (2001a,b; 2002), the report *Medication for older people* (Royal College of Physicians, 1997) and standard textbooks of clinical pharmacology are recommended.

In brief, progressive changes take place with advancing age, such that reduced liver blood flow and function results in decreased hepatic drug metabolism. The number of functional nephrons in the kidney decreases along with renal blood flow and by the age of 70, renal function is likely to be, at best, only 50% of its original maximum (McGavock, 2002). The duration of action of a drug is commonly described by referring to its elimination half-life ($t_{1/2}$). It is important to remember that this is only the time it takes for the drug-concentration in the plasma to reduce to half its previous value. Whether or not a drug still has significant effects at the end of one, two or more half-lives will depend on whereabouts on the dose-response curve the therapeutic dose range has been set, as well as on individual patient responsiveness and complex pharmacokinetic considerations such as deviation from first-order kinetics. Particularly for lipophilic drugs, a significant amount may remain in the brain even after plasma concentrations have become undetectable.

Age-related decreases in lean-mass, body water and plasma binding-proteins, together with a likely increase in the proportion of fatty tissue all act to alter the way a drug is distributed in the body. The consequences of this depend largely on the individual physico-chemical properties of the drug in question, but in general more lipophobic drugs have a reduced volume of distribution in the elderly and are more likely to require dose reduction in this population. In general, changes in drug absorption are not significant in older people.

Changes in tissue responsiveness to drugs are difficult to disentangle from pharmacokinetic changes. Nevertheless, progressive loss of brain and peripheral neurones resulting in altered receptor density, impaired homeostatic mechanisms, loss of elasticity of connective tissue and impaired thermoregulation together with the greater likelihood of comorbidity, may all contribute to increased, or occasionally decreased, responsiveness.

All these changes show a wide variation and they affect some drugs more than others. It is also important to consider a patient's biological, as opposed to chronological age, especially where the former appears to be greater than the latter.

Older patients are more likely to be prescribed multiple medication. It has been suggested that a third of older patients have three or more chronic diseases (Brody et al., 1998) but consequent polypharmacy may be unavoidable. The more different medications that are being taken, the greater the likelihood of pharmacokinetic or pharmacological interactions. McGavock (2002) describes a hypothetical case where rational prescribing would result in a patient taking digoxin, a loop diuretic, an angiotensin converting enzyme (ACE) inhibitor, a low-dose cardioselective beta-blocker, Warfarin and a statin and quotes the risk of a serious adverse drug reaction with this combination as over 50%.

Partly due to such polypharmacy, concordance problems are more likely in the older patients and, as well as dose-omission, this may result in taking the medication too frequently or at inappropriate times of day. Finally, it must never be forgotten that patients may be dosing themselves with OTC medicines that may interact or have additive effects with those prescribed.

In prescribing for older patients:

- 'Biological' age and medical history should be taken into account.

- Guidelines for the prescription of individual drugs, such as those in the BNF, regarding dose reduction during initiation and continuation therapy are readily available and should be followed.

- Liver and renal function tests are a valuable aid to decision making and patient monitoring in cases of doubt.

- Polypharmacy should be reduced to the unavoidable minimum. Enquire and advise on self-medication including herbal products.

- Fixed-dose combination medications should be avoided where possible.

- Dosage regimens should be kept as simple as possible to aid concordance.

- A patient's status may change, and regular medication review is advisable.

5.4.1 The question of tolerance

The sedative effects of many medications appear to wear off over a period of continued use. The reasons for this include adaptations in physiological processes, changes in receptor density and, in some cases, induction of metabolising enzymes. This has led to an assumption that major driving impairments will occur only in the early stages of a course of treatment (see Linnoila & Seppala, 1985). This assumption is unsafe. Tolerance is not a unitary process, and can occur to different degrees for different neuropsychological attributes (Aranko et al., 1984; Stein & Strickland, 1998). For example, there are distinct differences in the extent of tolerance development to antihistamines between perceived drowsiness (extensive) and objective tests of performance (minor) (Gengo & Manning, 1990); no tolerance was detected on continued dosing to the psychomotor impairments induced by amitriptyline, whereas the sedative effects declined (Sakulisprong et al., 1991). Importantly, a pharmaco-epidemiological study carried out on older drivers in Quebec indicated little decrease in the risk of an RTA with continued (2-12 months) use of long half-life benzodiazepines as compared with short-term exposure (1-7 days) (Hemmelgarn et al., 1997).

These findings suggest that at least some neuropsychological impairment relevant to driving may continue, and that it would be insufficient to advise against driving only in the early phases of treatment with an impairing medication.

5.5 Anticholinergic effects and side-effects: general considerations

While a minority of medications are used primarily for their ability to block muscarinic cholinergic (Ach_M) receptors, anticholinergic side effects are widespread among many classes of medicines. In view of this, together with evidence that older people are more sensitive to the impairing effects of blocking these receptors, this topic will be dealt with separately, to avoid undue repetition.

5.5.1 Consequences of blocking Ach_M receptors

Blockade of Ach_M receptors has important central and peripheral consequences relevant to driving. Brain cholinergic neurones play an important role in normal cognitive function and arousal, and central consequences of cholinergic blockade can range from minor neuropsychological impairments to delirium (acute confusional state) (see Moore & O'Keeffe, 1999). Information-processing deficits include reduced ability to sustain or focus attention (Tune, 2000). Short-term memory as well as delayed recall can be affected (see Nebes et al., 1997).

Peripheral muscarinic blockade can affect visual acuity, by reducing accommodation of the lens as well as by causing mydriasis. Occurrence of tachycardia due to vagal block could act as a distractor. The possibility of acute urinary retention developing during a long journey, especially in older men with prostate problems, must not be forgotten. Nausea, vomiting and dizziness have also been recorded.

5.5.2 Sensitivity in older patients

Older patients are well known to be substantially more sensitive to the impairing effects of anticholinergic medications (Molchan et al., 1992; Moore & O'Keeffe, 1999; Tune, 2000, 2001; Zemishlany & Thorne, 1991). Markers for cholinergic neurones decrease with age and age-related loss of 'cholinergic reserve' is a major factor in this increased sensitivity (Tune, 2000). This evidence suggests that medications with anticholinergic properties should be regarded as an important risk to the older driver.

5.5.3 Effects of primary anticholinergic medications

Primary anticholinergic medications include those used for their bronchodilator, gastro-intestinal, urinary tract and anti-Parkinsonian properties, as well as those used topically for their effects on the eye. Quaternary compounds such as **ipatropium, oxitropium, propantheline, trospium** penetrate the blood-brain barrier poorly, and central effects appear not to have been recorded. However, it has been pointed out that this barrier is not absolute (Ramaekers & Vermeeren, 2000), so a potential contribution of such substances to cognitive impairment should still be borne in mind and these agents can have prominent peripheral actions. **Oxybutynin** has been noted as problematic (Moore & O'Keeffe, 1999) and **flavoxate** and **tolterodine** can cause CNS effects (BNF). **Benztropine, biperiden, orphenadrine, procyclidine** and **trihexphenidyl** are used for their effects on the brain in the relief of mild Parkinsonism and antipsychotic-induced pseudo-Parkinsonism and should thus be regarded as presenting a risk (Moore & O'Keefe, 1999). **Atropine, dicycloverine, hyoscine (scopolamine),** present problems (Moore & O'Keeffe, 1999). Systemic reactions to ocular antimuscarinics (**atropine, homatropine, cyclopentolate, tropicamide**) are a possibility in older patients (Barker & Solomon, 1990).

Neuropsychological impairment: Anticholinergic medications are well known for their ability to compromise performance in neuropsychological tests of cognitive function (see Moore & O'Keeffe, 1999). Indeed, hyoscine is widely used as a reference substance in human and animal studies of cognition and has been found to impair performance in attentional and vigilance tasks (Duka et al., 1996) and reaction time (Brandeis et al., 1992). However, a Medline search using the terms 'anticholinergic' and 'automobile driving' (1966-2002) failed to reveal any studies of the effects of primary anticholinergic medications on skills related to driving.

Epidemiological studies: Perhaps because of the relative rarity of their use, compared with psychotropic medications such as benzodiazepines and antidepressants, primary anticholinergic agents have not yet been searched for as a risk factor in epidemiological studies.

5.5.4 Anticholinergic side effects of other medications

Many medications have anticholinergic side effects. First-generation antidepressants, antipsychotics and antihistamines have the highest profile and their anticholinergic effects have repeatedly been suggested to make an important contribution to their ability to impair

driving performance (sections 5.5, 5.8). But many other agents, including OTC medications, possess at least weak anticholinergic properties or have metabolites with this property (Tune, 2000). Since older patients are more likely to be taking multiple medications (Nebes et al., 1997; Tune, 2001), the cumulative burden can easily become significant. Total 'serum anticholinergicity' (SA) may be measured in radioligand-binding assays and expressed as 'atropine equivalents' (Tune, 2000) and studies with this technique have revealed that significant cognitive effects are produced at comparatively low levels of SA (Tune, 2000). Older patients with a low SA (<1pMol atropine equivalent) performed worse on a delayed recall task than those with none (Nebes et al., 1997).

The SA of medications has been measured and cimetidine, prednisolone, theophylline, digoxin, nifedipine = furosemide = ranitidine (in descending rank order) were found among the worst 'offenders' (see Tune, 2000, for a complete list). These agents are not normally thought of as having anticholinergic effects, and this list illustrates the importance of considering the potential cumulative actions of all medications, including OTC that a patient may be taking.

While the anticholinergic side effects of older antipsychotics and tricyclic antidepressants are well recognised, two antipsychotic-related medicines frequently prescribed for older patients for other indications include metoclopramide and prochlorperazine. The potential additive anticholinergic risk to driving of these agents may be overlooked.

Overview

Medication used primarily for their anticholinergic actions (primary anticholinergic agents) present a major theoretical risk to driving ability that is likely to be substantially greater in older patients. Anticholinergic side effects may play an important role in the risk of driving impairment produced by antidepressants, antihistamines and antipsychotics. The total anticholinergic burden produced by multiple medications must be borne in mind. Wherever possible, medications with lesser anticholinergic activity should be chosen for the older driver.

5.6 Antihistamines (H$_1$ antagonists)

Sedating, or first-generation antihistamines: **trimeprazine, azatadine, brompheniramine, chlorpheniramine, clemastine, cyproheptadine, diphenhydramine, diphenylpyraline, doxylamine, hydroxyxine, pheniramine, promethazine, triprolidine**. Warning label 2.

Non-sedating or second-generation antihistamines: **acrivastine, cetirazine, fexofenadine, loratadine, mizolastine, terfenadine**. No warning label, counselling advised with respect to driving. **Emedastine** is currently available as eye-drops for seasonal conjunctivitis but is reported as being under consideration for licensing as an oral antihistamine in Europe (Vermeeren et al., 2002).

Histamine is a substance endogenous to the central nervous system and acts as a neurotransmitter in a minority of brain neurones. It appears to be important to cortical arousal and antihistamines that penetrate the CNS are well known to cause sedation. The

older, first-generation antihistamines also commonly possess anticholinergic and alpha$_1$-anti-adrenergic properties (Meltzer, 1990). In recent years, the emphasis has been on producing agents that are less lipophilic and thus penetrate the blood-brain barrier only poorly, these agents are also more specific for histamine H$_1$ receptors. However, even these newer agents cannot be regarded as entirely free of CNS adverse effects (Horak & Stubner, 1999; O'Hanlon & Ramaekers, 1995; Mann et al., 2000, Ramaekers & Vermeeren, 2000. Terfenadine (and to a lesser extent, astemizole) has been associated with potentially fatal cardiac arrhythmias, especially in the presence of hepatic impairment or of other medications that inhibit its metabolism to fexofenadine and thus increase its level in the plasma; this association with hepatic impairment is particularly relevant to older patients.

Older people are reported to be more susceptible to the sedating and anticholinergic effects of both first and second-generation antihistamines (McCue, 1996).

Neuropsychological tests: Detailed reviews of the effects of antihistamines in neuropsychological tests (Ray et al., 1993 and Gemmell et al., 1999) indicate that deficits occur after acute administration of therapeutically relevant doses of first-generation agents. Performance decrements have been reported in a variety of tests including visuo-motor coordination, dynamic visual acuity and attentional tasks. Diphenhydramine produced a greater impact than ethanol in a driving simulator, whereas fexofenadine and cetirazine were without effect (Weiler et al., 2000; Gengo & Manning, 1990).

On-road driving: There have been extensive experimental studies of actual driving under the influence of antihistamines. Among first-generation antihistamines, adverse effects have been looked for, and found with triprolidine and diphenhydramine, (O'Hanlon & Ramaekers, 1995). Concerning second-generation agents, single-dose studies indicated mizolastine had no effect at the recommended therapeutic dose of 10mg but impairment equivalent to 0.8mg/ml blood ethanol was recorded at 20-40mg (Vuurman et al., 1991) and O'Hanlon & Ramaekers (1995) regarded their data as showing that impairment begins after 'about 10mg' of this agent. Loratidine was also without effect at the 10mg daily therapeutic dose but caused significant impairment when given at higher doses and/or more frequently (O'Hanlon & Ramaekers, 1995). For acrivastine, the recommended dosage is 8mg three times daily and, at this level, it produced no changes over 4 days of dosing in male volunteers, but females were significantly impaired (O'Hanlon & Ramaekers, 1995) and higher doses impaired both sexes. Results with cetirazine have been variable, perhaps due to varying proportions of females in study samples (O'Hanlon & Ramaekers, 1995). In a recent study in which cetirazine 10mg daily over 5 days was used as a reference compound, no significant effects were seen with male volunteers, but females were significantly impaired on day 4, although this effect was not significant in combination with ethanol on day 5 (Vermeeren et al., 2002). In contrast, emedastine (2 or 4mg twice daily) in the same study caused severe impairment; this impairment was greater in females and seven subjects were stopped from driving with emedastine compared with two on cetirazine and one on placebo (Vermeeren et al., 2002). Several other agents may be more impairing in females, including acrivastine (O'Hanlon & Ramaekers, 1995; Robbe & O'Hanlon, 1990), cetirazine (O'Hanlon & Ramaekers, 1995; Vermeeren et al., 2002) and mizolastine (Vuurman et al., 1994). Whether this is a general property of antihistamines or applies only to this group of structurally related compounds is unknown.

Perceived sedation: Several studies have examined perceived sedation/drowsiness produced by antihistamines and concluded that it is a poor indicator of driving-related impairment (Gengo & Manning, 1990; Weiler et al., 2000; O'Hanlon & Ramaekers, 1995). The question of tolerance has not been fully addressed, but there are indications that the occurrence of tolerance to driving impairment-related properties of antihistamines may not be complete (Gengo & Manning, 1990).

Epidemiological studies: Antihistamines are less often included in epidemiological studies, largely because many of them are available OTC without the need for a prescription (Maes et al., 1999). Neither the 'Tayside' (Barbone et al., 1998) nor the 'Saskatchewan' (Neutel, 1995) pharmaco-epidemiological studies included antihistamines in their substances of interest. Skegg et al. (1979) found a non-significant increase in relative risk of 1.8 for car drivers although the risk was significantly increased for motorcyclists. Hydroxyzine was found 8 times more frequently than expected by chance in blood samples obtained from fatally injured drivers in Sweden (Johansson et al., 1997). Mann et al. (2000) used prescription-event monitoring to examine sedation caused by four recently introduced antihistamines: loratidine, cetirazine, fexofenadine and acrivastine, finding no increased risk of accident (including road traffic accident, which was analysed separately) with any of these compounds. Interestingly, they did discover significantly more reports of sedation or drowsiness with cetirazine and acrivastine, commenting 'in situations where even very infrequent reports of sedation are undesirable (for example when prescribing for flight crew) loratadine or fexofenadine are preferable to acrivastine or cetirazine'.

In the Seattle-based pharmaco-epidemiological study of older drivers (Levieille et al., 1994), current exposure to antihistamines was not associated with an increased risk of being involved in a collision and, perversely, those cases with a lower probability of exposure appeared at higher risk (OR 1.9-2.0) than those with the highest probability (OR 0.6). The authors suggested this may have been a spurious finding since it did not recur in a sub-analysis of 'at fault' drivers. They also point out that diphenhydramine, accounting for 80% of antihistamine use in their study, is available OTC, so could have been taken by control subjects. In view of the evidence quoted above, that females are more sensitive to impairing effects of antihistamines, it would be interesting to know the relative proportion of females in the different exposure groups in this study. The 'Tennessee' study indicated a 20% increase in risk among older drivers currently taking antihistamines, which was not statistically significant (Ray et al., 1992).

Overview

Tests of actual driving, as well as neuropsychological tests, indicate a risk of driving-related impairment with first-generation, sedating antihistamines. It is not established that complete tolerance occurs to these effects. The risk in females may be higher than it is in males and good evidence for this distinction has been found among second-generation 'non-sedating' antihistamines. The absence of confirmation in epidemiological studies indicates a lack of evidence, rather than evidence for a lack of risk. Since older patients are more sensitive to the impairing effects of antihistamines, it may be presumed that their risk is greater. Wherever possible, second-generation antihistamines should be chosen but should not be

assumed to be entirely risk-free. When prescribing other medications for older patients that may affect driving ability, enquiry should be made on use, choice and dosing frequency of OTC antihistamines and patients should be advised on the possibility that at least additive effects of such agents cannot be excluded on current evidence. It would also be appropriate to advise that perceived sedation is not a good indicator of potential driving impairment.

5.7 Anxiolytics

Benzodiazepines: **alprazolam X; bromazepam X; chlordiazepoxide; clorazepate X, lorazepam, oxazepam.** X – not available for NHS prescribing. Warning label 2.

Benzodiazepine-like: **meprobamate** (CD not recommended – BNF). Warning label 2.

Buspirone (**No warning label; counselling on driving – BNF**).

Antihistamines licensed for the treatment of anxiety are covered in the section on antihistamines.

Beta-blockers licensed for the treatment of anxiety are covered under cardiovascular medications.

SSRIs licensed for the treatment of anxiety are covered under antidepressants.

5.7.1 Benzodiazepines

Benzodiazepines are indicated for the short-term relief (2-4 weeks) of severe or disabling anxiety (Committee on the Safety of Medicines< as described in the British National Formulary). Moderate to long half-life compounds are used to allow a suitable dosing frequency, however, the risk of excessive and/or cumulative effects should be borne in mind in older patients, due to known pharmacokinetic changes (Ray et al., 1992) and appropriate dose adjustments made (BNF). Importantly, benzodiazepines have been identified as a major contributor to acute confusional states and chronic cognitive impairment (pseudodementia) in older patients (Moore & O'Keeffe, 1999).

Neuropsychological tests: There is strong evidence that anxiolytic benzodiazepines cause impairment in cognitive and psychomotor functions related to driving (Gemmell et al., 1999; Ray et al., 1992; Hindmarch, 1986). These agents are sedative, amnestic and muscle-relaxant and anticonvulsant, due to their ability to potentiate the effects of the neurotransmitter gamma-aminobutyric acid (GABA) at the $GABA_A$ receptor. Thus, it is not surprising that significant effects have been noted in many tests including vision, attention, information-processing, memory and motor coordination (reviewed in Gemmell et al., 1999; Ray et al., 1992; Stein & Strickland, 1998): older people are more sensitive to the effects of a given dose. The degree of residual impairment also increases with age and effects last for at least the period of 2-4 weeks over which benzodiazepine prescribing is advised (see Ray et al., 1992).

Risk-taking: Benzodiazepines can disinhibit behaviour and increase impulsiveness; this can result in increased willingness to take risks (reviewed in van der Bijl & Roelofse, 1991). This is an ethanol-like effect: like benzodiazepines, ethanol also increases chloride transfer through the $GABA_A$-associated chloride ion channel.

On-road driving: Controlled driving studies have consistently indicated driving deficits in patients taking benzodiazepines (O'Hanlon et al., 1982; O'Hanlon & Volkerts, 1986; Ray et al., 1992; O'Hanlon et al., 1995).

Epidemiological studies: Benzodiazepines as a class have shown to consistently increase the risk of being involved in an RTA (Skegg et al., 1979; Ray et al 1992; Hemmelgarn et al., 1997; Barbone et al., 1998; Neutel, 1995; Leveille et al., 1994; Oster et al., 1990; McGwin et al., 2000). Those studies that have examined benzodiazepines by indication have also detected that benzodiazepine anxiolytics have a higher risk than benzodiazepine hypnotics (Hemmelgarn et al., 1997; Barbone et al., 1998; Neutel, 1995). Where duration of treatment has been examined, Neutel (1995) found a very high risk in the first week after prescription of an anxiolytic benzodiazepine (OR 13.5), falling substantially (OR 1.2) by the second month, while Hemmelgarn et al. (1997) found an initial risk of 1.45 that remained up to a year. There was evidence of a dose-dependent effect in the Tayside study (Barbone et al., 1998).

Several of these studies referred only to older patients (Leveille et al., 1994; Ray et al., 1992; Hemmelgarn et al., 1997) and found an increased risk of RTA involvement with benzodiazepine use. However, two studies compared different age groups and neither of these suggests older patients to be at greater risk than the population as a whole (Barbone, 1998; Neutel, 1995). Indeed, the Tayside study (Barbone et al., 1998) found an inverse relationship with age, and suggested that perhaps this could be an artefact of their design or, alternatively, that older people were less likely to drive early in a course of treatment.

Could the excess risk of an RTA under the influence of anxiolytic benzodiazepines be due to the condition for which they were prescribed, rather than the treatment itself? Anxiety disorders, stress etc. does appear to increase vulnerability to RTA (section 4.2.5.3). Neutel (1995) considered the factors consistent with medication risk to be stronger than those factors associated with the disorder for which the medication was prescribed. The Tayside group (Barbone et al., 1998) point out that anxiolytic benzodiazepines are prescribed for a wide range of reasons, not just for an anxiety disorder, and felt that the clear dose-response relationship seen in their study was strong evidence for a medication effect.

5.7.2 Buspirone

Buspirone is unrelated to benzodiazepines both in its structure and mechanism of action, being a $5-HT_{1A}$ receptor partial agonist. It does not cause overt sedation. Unlike the benzodiazepines, the onset of its therapeutic action is delayed and 'nervousness' may occur during the initial lag-phase (manufacturer's patient information insert).

Neuropsychological tests: The recommended dose-range for buspirone is 5-15mg three times daily. In contrast to diazepam, acute treatment with buspirone 5mg had no effect on disengagement of attention as measured by saccadic eye movements (Fafrowicz et al., 1995), or (at 15mg) on memory, psychomotor performance and alertness (Unrug-Neervort et al., 1992). Older volunteers were also unaffected, both acutely (Lawlor et al., 1992) and in a study with 14-day crossover segments of buspirone 5mg three times a day versus placebo and alprazolam (Hart et al., 1991). In contrast, a single dose of buspirone 10mg did disturb performance in free recall and in a digit/symbol substitution test, but CFF and choice-reaction time were unaffected (Bourin et al., 1989). In a driving simulator, buspirone 20mg daily for 9 days improved performance, both immediately and on the eighth day of treatment, while diazepam, given as a reference drug, caused extensive impairment throughout (Moskowitz & Smiley, 1982).

On-road driving: Buspirone 5 or 10mg three times in one day caused a small (equivalent to less than 0.5mg/ml blood alcohol concentration) but statistically significant deterioration in driving (SDLP) in a cross-over study in which lorazepam (3 doses of 1mg) caused severe impairment (Volkerts et al., 1987). In a study by van Laar et al., (1992), buspirone (5mg tid) caused no detectable impairment in anxious outpatients in a crossover design (7-day segments) with diazepam as the reference compound.

Epidemiological studies: Buspirone has not been investigated in epidemiological studies.

Overview

Persons suffering from severe, disabling or distressing anxiety, for whom anxiolytic benzodiazepines may be appropriate (Committee on Safety of Medicines), should be advised of the driving risks inherent in their condition (section 4.2.5.3). However, anxiolytic benzodiazepines present a risk to driving that is likely to be independent of the condition for which they are prescribed. While there is reason to believe that older people may be more sensitive to the impairing effects of benzodiazepines, appropriate dose and regimen adjustments are intended to negate this effect and the prediction of an increased risk to older people has not yet been supported by epidemiological studies. Nevertheless, the evidence of overall increased risk to driving is strong and some studies suggest this increase does not disappear with time. Patients of all ages prescribed an anxiolytic benzodiazepine should be informed of these risks and advice against driving is appropriate.

Newer agents are now available for the treatment of anxiety disorders. Experimental studies suggest buspirone may be a safer alternative but initial exacerbation of anxiety can occur and counselling on driving is advised (BNF). SSRIs are now licensed for treatment of some anxiety disorders, but are considered under antidepressants in this context (section 5.8).

5.8 Hypnotics

Benzodiazepines and benzodiazepine receptor agonists: **nitrazepam X, flunitrazepam X, flurazepam X, loprazolam X, lormetazolam, temazepam, zaleplon, zolpidem, zopiclone.** X: not available for NHS prescribing. Label 19 except zaleplon, label 2.

Other hypnotics: **Cloral hydrate N, triclofos N, clomethiazole** are considered less suitable for prescribing, (BNF) label 19.

Sedative antihistamines: see section 5.5.

The aim of hypnotic medication is to induce and/or maintain sleep. The focus of interest so far as driving is concerned is whether residual affects occur the following day. Recent emphasis has been on the development of compounds with a shorter duration of action and thus with less predicted likelihood of causing residual impairment: zaleplon, zolpidem and zopiclone, while non-benzodiazepine in structure, exert their hypnotic effects by acting on benzodiazepine receptors. This is likely to change prescribing trends, and current epidemiological data may not accurately reflect this developing situation. For this reason, individual hypnotic agents have been examined in some detail. Benzodiazepine-treatment of insomnia is recommended only when it is severe, disabling or subjecting the individual to extreme distress (Committee on the Safety of Medicines).

Neuropsychological tests: The vast majority of these are single-dose studies, with none extending beyond one week. When taken at night, residual impairment has been consistently reported to occur after therapeutic doses of flunitrazepam, flurazepam, loprazolam and nitrazepam (Bocca et al., 2000; Bensimon et al., 1990; Elie et al., 1990; Grobler et al., 2000; Harrison et al., 1985; Morgan et al., 1984; Moskovicz et al., 1990; Murakoa et al., 1992; Ott et al., 1988; Richens et al., 1993; Sicard et al., 1993; Schmidt et al., 1986; Stanley et al., 1987; Tornos & Laurel, 1990; Woo et al., 1991). A study of lormetazepam (therapeutic range 0.5-1.5mg, BNF) suggested impairment following 2mg but not after 1mg (Ott et al., 1988). No data appears available on chloral hydrate or tricoflos; a single study of chlomethiazole indicated no impairment after 384mg on 5 successive nights, and was carried out in an older sample (Liljenberg et al., 1986).

Temazepam and zolpidem at therapeutic doses consistently failed to produce residual impairment (Bensimon et al., 1990; Hemmeter et al., 2000; 1990; Nakra et al., 1992; Richens et al., 1993; Schmidt et al., 1986; Sicard et al., 1993; Stanley et al., 1987; Troy et al., 2000; Volkerts et al., (2000). The study by Bocca et al., (2000) however, indicated an alteration in visual processing. Therapeutic doses of Zopiclone also failed to induce residual impairment in the majority of studies (Billiard et al., 1987; Elie et al., 1990; Grobler et al., 2000; Hemmeter et al., 2000; Subhan & Hindmarch, 1984; Tafti et al., 1992), although impairment was detected in studies by Lader & Denney, (1982), Nicholson & Stone, (1982) and Vanmeeren et al., (2000). Residual impairments have not been observed after therapeutic doses of zaleplon taken at bedtime (Hindmarch et al., 2000; Troy et al., 2000; Vermeeren et al., 2000; Volkerts et al., 2000) although a deficit was revealed in the digit-symbol substitution test when taken one hour before morning waking (Hindmarch et al., 2000).

Studies on older participants produced the same pattern: residual impairment after flurazepam 15mg (Woo et al., 1991), no residual impairment after temazepam 15-20mg (Hemmeter et al., 2000; Nakra et al., 1992) or zolpidem 10mg, although impairment was observed after 20mg zolpidem which is twice the recommended dose (Troy et al., 2000).

On-road driving: There have been relatively few studies of the residual effects of therapeutic doses of hypnotics on actual driving. Temazepam and flurazepam were compared for their effects on road driving by sleep-disorder patients the morning after first and seventh bedtime doses; flurazepam caused significant impairments on both occasions while temazepam produced an apparent overall improvement after the first dose but a significant decrease in one parameter after the seventh. (Schmidt et al., 1986). In a study by Vermeeren et al., (2000), driving performance was not affected 10 hours after zaleplon 10mg, but zopiclone (7.5mg) caused significant impairment. A further study (Volkerts et al., 2000) assessed zaleplon (10 and 20mg) effects 4 hours after a dose given in the middle of the night; again no impairment was detected in driving performance, although zolpidem (10 and 20mg given at this time) caused significant impairment.

Pharmaco-epidemiological studies: Three studies have distinguished benzodiazepines used as hypnotics from those used as anxiolytics. In the Tayside study (Barbone et al., 1998), this distinction was made according to the British National Formulary. Overall, benzodiazepine hypnotics presented a marginally elevated risk of a police-attended RTA (OR 1.19) and one substance stood out as individually increasing the risk: zopiclone (OR 4.0). The authors were very clear in their conclusion: users of zopiclone should be advised not to drive. It is interesting to note that, although zopiclone caused detectable impairment of on-road driving (Vermeeren et al., 2000), neuropsychological impairments were noted only in a minority of studies (see above). This finding suggests on-road driving experiments may be better predictors of risk than neuropsychological tests. The Tayside group (Barbone et al., 1998) also analysed their data by age and did not detect the elderly to be at any greater risk than other age groups after prescription of hypnotic benzodiazepines.

The Saskatchewan study (Neutel, 1995; 1998) also stratified the benzodiazepine data by indication. The hypnotic benzodiazepines were flurazepam and triazolam, and they found a more than four-fold increase in risk of hospitalisation following an RTA of 4.9 per 10,000 (controls 1.2 per 10,000). Again, older drivers did not appear to be at increased risk, in fact their risk was lower at 2.8 per 10,000. The all age-group risk decreased with time since prescription (from an OR of 9.1 in week 1 to 1.4 in weeks 5-8; Neutel, 1995).

In the Quebec study (Hemmelgarn et al., 1997), benzodiazepines were categorised into half-life longer or shorter than 24 hours, which does not map well to UK hypnotic versus anxiolytic categories (shorter half life were alprazolam, bromazepam, lorazepam, oxazepam, temazepam, triazolam); shorter half-life compounds did not show an increased risk of RTA involvement, whether prescribed for 1 week or up to 1 year.

Night-time impairment: The pharmacodynamics of hypnotic agents are similar to those of the anxiolytic benzodiazepines and similar impairments would be expected. Neuropsychological studies that have examined effects of hypnotics in the early period after ingestion have borne this out (Hindmarch et al., 2000).

Dose-dependency: The Tayside study of police-attended RTA found risk to be dose-dependent when dose-range was stratified by BNF recommendations (Barbone et al., 1998).

Half-life dependency: Half-life is only a surrogate indicator of duration of action, useful for standardising comparisons between agents (see Section 5.3). The contrast between the apparent relative safety of temazepam (total elimination half-life 8-15 hours including active metabolites) versus zopiclone (6.5 hours) illustrates the pitfalls of using this measure to predict risk. Nevertheless, Hemmelgarn et al., (1997) found a greater risk of RTA involvement in the elderly after long (>24 hours), as opposed to short (<24 hours) half-life benzodiazepines in general, especially early in treatment. The Tayside study (Barbone et al., 1998) detected a different pattern: short half-life hypnotics exhibited a higher risk than intermediate- and long-acting ones, however, all the short half-life incidents involved patients who had taken zopiclone (6.5 hours). In the Saskatchewan study, the long-acting flurazepam (47-100 hour) appeared a very high risk (all ages OR 5.1), decreasing somewhat to OR 3.4 in the over 60's but the very short-acting hypnotic triazolam (OR 3.2) presented the same level of risk to 'new' users (within 4 weeks of first prescription) as the very long-acting anxiolytic benzodiazepine, diazepam (OR 3.1) (Neutel, 1998) and the degree of risk appeared similar in the elderly (OR 2.9). Half-life thus appears a poor indicator of risk.

Impairing effects of insomnia versus its drug treatment: Sleep deprivation can impair skills related to driving (section 5.2.4) and this risk can, on occasion, be severe as evidenced by the Selby rail crash. There is insufficient evidence to determine whether this risk is altered by effective treatment with hypnotics as a class.

Overview

There is a paucity of on-road driving studies examining the residual effects of hypnotics and recent introductions mean that pharmaco-epidemiological studies may not adequately represent current risks. Risk detection therefore places more reliance on neuropsychological studies than for many other medication classes and in the main these have been single-dose studies. These studies indicate, overall, that risks are higher for older, longer half-life agents. Nevertheless, epidemiological studies indicate that shorter half-life does not guarantee lack of risk and one agent, zopiclone, has stood out as increasing the risk of involvement in a road traffic accident. The risk may also be greater early in a course of treatment.

Hypnotic benzodiazepines should be prescribed with caution for drivers of all age groups. Although current evidence suggests the elderly are not at increased risk compared with younger people, prescribing for this group must rely on individual patient assessment and dose should be adjusted according to available guidelines.

All patients should be warned of the risks to driving 'during the night' once a hypnotic agent has been taken.

5.9 Antidepressants

Tricyclic and related antidepressants (TCAs): **amitriptyline, amoxapine, clomipramine, dosulepin (dothiepin), doxepin, imipramine, lofepramine, nortriptyline, trimipramine, maprotiline, mianserin, trazodone** (warning label 2).

Monoamine oxidase inhibitors (MAOIs): **phenelzine, isocarboxazid, tranylcypromine**. Not recommended (BNF), (warning label 3).

Reversible monoamine oxidase inhibitor: **moclobemide.**

Selective serotonin reuptake inhibitors (SSRIs): **citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline** (counselling on driving).

Other antidepressant drugs: **mirtazepine** (2), **nefazodone** (3), **reboxetine** (counselling), **venlafaxine** (counselling), **tryptophan** (3) (warning label see individual agents).

flupenthixol: (see antipsychotics).

Antidepressants are used relatively long-term in the treatment of depression and some are also licensed for anxiety and related disorders. All share a common characteristic of a lag of 1-3 weeks before onset of their therapeutic action and a further several weeks before it is fully developed. Their safety in the older patients is an important issue since depression is relatively more common in this age group (see section 4.2.5.3 above).

Antidepressants are not curative agents, rather they are used to remove the symptoms of a current depressive episode. Depression itself can cause important neuropsychological impairment, including retardation of cognitive and motoric functions that can affect driving (see section 5.2.6) so, for these agents, the interactions between the disease and its treatments is an issue that requires consideration (Edwards, 1995). There have been a number of recent advances in the treatment of depression, particularly in the development of antidepressants with an improved side effect profile due to the greater specificity of their actions: selective serotonin reuptake inhibitors (SSRIs), mixed reuptake inhibitors (venlafaxine, nefazodone, noradrenaline-specific reuptake inhibitors (reboxetine), alpha$_2$-adrenoceptor antagonists (mirtazepine) and reversible monoamine oxidase inhibitors (RIMAS) (moclobemide). These have barely been available long enough to be detected as drug classes in pharmaco-epidemiological studies, generating a greater reliance on experimental studies.

Low-circulating sodium levels (hyponatraemia) may occur after any type of antidepressant, especially in older patients, and may lead to drowsiness, confusion or convulsions (Committee on Safety of Medicines).

For clarity, the main classes of antidepressant will be evaluated separately.

5.9.1 Tricyclic antidepressants (TCAs)

This is a group of older antidepressants: noradrenaline- or noradrenaline and serotonin-reuptake inhibitors characterised by prominent side effects due to blockade of cholinergic (Ach_M), histamine (H_1) and $alpha_1$ receptors. Since anticholinergic (section 5.4) and antihistaminic (section 5.5) actions impair neuropsychological functions relevant to driving, significant risk to driving is predicted for this drug class. This may be especially true of the elderly, since this patient group appears particularly sensitive to these effects.

Neuropsychological tests: The effects of TCAs on neuropsychological function in healthy volunteers have been widely studied and reviewed. There is a clear consensus that neuropsychological impairment occurs at normal therapeutic doses, and that this does not completely disappear with continued dosing (reviewed by Ray et al., 1993; Stein & Strickland, 1998; Amado-Boccara et al., 1995; Gemmell, 1999; Maes et al., 1999). The more sedative agents, such as amitriptyline and dosulepine, produce the greatest deficits.

Several studies have been carried out in depressed patients. In general, those highly sedating antidepressants that produce adverse effects in healthy adults show the same pattern in clinical populations (Stein & Strickland, 1998). After reviewing the relevant studies, Ray et al., (1993) considered that TCAs decrease, rather than improve function in depressed patients. Li et al., (1996) studied a variety of balance and weight-shifting functions in patients medicated for depression for more than a year, pointing out that previous work has indicated that antidepressants can affect these functions. Treatment with TCAs (amitriptyline and doxepin 50mg) significantly affected motor coordination, fine-motor control, postural reflexes and reaction time. The length of treatment suggests these changes are likely to be traceable to the medication rather than the underlying condition particularly since SSRIs did not produce these effects.

Studies in elderly patients suggest this patient group to be consistently impaired by TCAs (Ray et al., 1993; Moore & O'Keeffe, 1999; Knegtering et al., 1994) although whether this reflects a true age-related increase in sensitivity or heightened concern is unknown (Ray et al., 1993) and comparative studies are lacking. Overall, older patients are at increased risk of adverse drug reactions after TCAs (Pollock, 1999). Sedative or anticholinergic antidepressants should be prescribed carefully to older people since their premorbid cognitive function may be precarious (Stein & Strickland, 1998).

On-road driving: Amitriptyline and doxepin (75mg in divided doses) produced deterioration in lateral position control comparable with 0.1% blood alcohol concentration (Louwerens et al., 1986). Imipramine (50mg twice daily 7 days) also reduced lateral position control (van Laar et al., 1995). Mianserin (30mg single dose) increased brake-reaction time (Ridout & Hindmarch, 2001) and 10-20mg 3 times daily for 15 days profoundly and consistently impaired driving (O'Hanlon et al., 1998); although this effect was greatest on day one, it was still significant on day fifteen. However, dosulepin (75 increasing to 150mg daily for twenty two days) did not significantly affect driving performance despite subjective reports of sedation (Ramaekers et al., 1995).

Pharmaco-epidemiological studies: In the Tayside study (Barbone et al., 1998), no overall increase in risk of police-attended RTA was detected but the stratified analyses indicated a very different position in the elderly, with an odds ratio of 2.06. Over all age groups, risk was dose-related with an OR of 1.39 for 'high' (BNF) doses. This is in agreement with the Tennessee study (Ray et al., 1992), which detected an overall relative risk of 2.2 in an elderly population rising to 5.5 in the highest-dose group. This latter study also found a tendency for risk to increase with duration of use beyond 30 days.

5.9.2 Selective serotonin reuptake inhibitors (SSRIs)

The agents in this class are highly selective for the serotonin transporter and have negligible activity for other receptors with the exception of a marginal anticholinergic activity with paroxetine (Boyer & Blumhart, 1992). They have an improved safety and tolerability profile in older patients compared with TCAs (Montgomery, 1998). The theoretical risk to driving is thus much lower than with TCAs. However, in the therapeutic dose-range, they will have greater effects at the serotonin transporter than will mixed reuptake inhibitors such as the TCAs, and this may present its own problems. Excessive blockade of serotonin reuptake can cause a toxic condition (serotonin syndrome) that can include clouding of consciousness, and there are relatively rare reports of extra-pyramidal side effects such as pseudo-Parkinsonism and akathisia due to serotonergic reduction of dopamine release (Gerber & Lynd, 1998). It has also been suggested that, since serotonin is integrally involved in sensory information-processing, potentiation of serotonergic transmission may be able to attenuate the effects of exteroceptive stimuli on arousal, and this could become significant under monotonous driving conditions (O'Hanlon et al., 1998).

Neuropsychological tests: As a group, SSRIs have very much less effect on psychomotor function than TCAs (Hale, 1994), Stein & Strickland, 1998). Amado-Boccara et al., (1992) reviewing the cognitive impact of single doses of antidepressants in healthy volunteers noted fluoxetine and sertraline to have no effect and paroxetine to impair function only at higher therapeutic doses (40mg), indeed improvements were noted in some studies despite reports of perceived drowsiness; Eight days treatment with paroxetine 20mg was without effect but deficits were noted at 40mg (Robbe & O'Hanlon, 1995). However, a more recent study of the neuropsychological effects of fluoxetine found 20mg daily to slightly reduce sustained attention over 22 days administration (Ramaekers et al., 1995). A review of the properties of sertraline suggest that it does not impair psychomotor function including simulated driving (Warrington, 1991). Fluvoxamine (50-100mg) was without effect in a single dose study (Fairweather et al., 1996) and 100mg did not affect saccadic eye-movements (Wilson et al., 2000). Citalopram improved several psychomotor measures including sustained attention (Nathan et al., 2000).

There is little evidence concerning the effects of SSRIs on psychomotor function in clinical populations (Stein & Strickland, 1998). A study on slowing of psychomotor functions in major depression (compared with untreated normal controls) indicated that depression-related retardation in primarily cognitive tasks had disappeared by the sixth week of fluoxetine treatment but slowing of motor processes was unchanged (Sabbe et al., 1996).

The tasks involved fine-motor control during copying and drawing so it is not clear how they would translate to the more gross movements involved in driving. A further study (Li et al., 1996) indicated that long-term treatment of depressed patients with SSRIs (fluoxetine 20mg or sertraline 50mg daily) did not cause any disturbances of balance, posture, reaction time or fine-motor control while TCAs caused significant deficits in these measures.

On-road driving: Fluoxetine (20mg daily for 22 days) did not affect driving performance (Ramaekers et al., 1995). Neither did paroxetine (20 and 40mg/day, Robbe & O'Hanlon, 1995).

Pharmaco-epidemiological studies: Because they are a relatively recent introduction, SSRIs have so far been examined as potential contributors to road accidents only in one study (Barbone et al., 1998). The mixed reuptake inhibitors nefazodone and venlafaxine were included with the SSRIs in this study. Overall, there was no evidence of an increased risk (OR 0.85) but the authors point out this was the smallest group of drug users in their study. Interestingly, the odds ratio increased when SSRIs were compared by dose (BNF recommendations) from 0.8 in the low dose group to 1.37 at intermediate doses (no data for high dose). In contrast to TCAs, the odds ratio was lower (0.41) in the elderly. Use of SSRIs is increasing and it remains to be seen whether their safety profile is maintained in future studies.

5.9.3 Monoamine Oxidase Inhibitors (MAOIs)

The irreversible MAOIs are now generally reserved for some patients not responding to other treatments. So far as driving is concerned, there is the risk of a sudden onset of impairment due to a drug or dietary interaction commonly known as the 'cheese syndrome'. Symptoms of this potentially fatal syndrome can include headache, blood-pressure elevation that can be extreme, cardiac arrhythmias, convulsions and coma. All patients should receive detailed advice on foods and medicines to avoid. Moclobemide, a reversible inhibitor of monoamine oxidase-A, appears to be free of this problem.

Neuropsychological tests: Studies on normal volunteers are essentially absent for irreversible monoamine oxidase inhibitors (Stein & Strickland, 1998). Research on clinical populations has focused on the elderly; typically they have revealed no cognitive deficits but the studies have been subject to methodological concerns (Stein & Strickland, 1998).

Studies with moclobemide are conflicting. It has been found to have a beneficial effect on cognitive function in older patients (Fitton et al., 1993; at (200mg daily for 8 days) and at 200mg twice daily for 8 days it did not alter motor or attention capacities (Ramaekers et al., 1992). However, treatment of depressed patients for 28 days resulted in a deterioration in psychomotor performance without amelioration of their depressive symptoms (Classen & Laux, 1990).

On-road driving: No experimental studies of the effects of irreversible MAOIs on driving were found. Moclobemide (200mg daily for 8 days) did not alter car-driving skills (Ramaekers et al., 1992).

Pharmaco-epidemiological studies: Monoamine oxidase inhibitors have not yet been target medications in a pharmaco-epidemiological study.

5.9.4 Other antidepressant agents

Nefazodone (100-200mg daily for 7 days) has produced psychomotor impairment, minor on day one but more obvious on day seven, in both younger and elderly volunteers (van Laar et al., 1995). When 200 or 400mg/day were administered for 8 days to healthy volunteers, nefazodone impaired CFF but improved measures of complex memory performance (Frewer & Lader, 1993).

Reboxetine (4mg) did not affect psychomotor function, including brake-reaction time (Hindmarch, 1997; Kerr et al., 1996).

Mirtazepine's anticholinergic effects are less marked than those of TCAs, but further research is required in the elderly (Holm & Markham, 1999). Drowsiness and sedation are reported to be transient (Montgomery, 1995).

Venlafaxine lacks anticholinergic and antihistaminic activity; its tolerability and safety appear unaltered in older patients (Rudolph & Derivan, 1996; O'Hanlon et al., 1998). It had little if any effect on road-driving performance over the first week of treatment (75mg daily) and none after the dose was increased to 150mg daily; these doses also had no effect in psychomotor tests except for one test of vigilance performance (O'Hanlon et al., 1998).

Tryptophan caused early morning sedative effects, as detected by EEG, after a single dose of 2G at night, but no psychomotor deficits were observed (Thorleifsdottir et al., 1989). Six nights' administration of 3G also failed to impair performance (Spiweber, 1986).

Overview

TCAs and related agents can impair skills related to driving. This impairment translates into poorer performance in on-road driving tests. Some evidence suggests the elderly may be more sensitive to these effects and this prediction was confirmed in a UK study of actual road accident involvement. The risk to driving may not lessen with duration of use. Many prescribing guidelines no longer put TCAs as first-line treatments for depression, especially in the elderly (e.g., The South London and Maudsley NHS Trust Prescribing Guidelines: 2001). SSRIs have much weaker effects than TCAs on neuropsychological functions related to driving. However, gastrointestinal side effects could act as distractors, especially early in treatment, and there is a rare risk of toxic syndromes. There may be a risk of inattention to external stimuli under monotonous driving conditions. SSRIs did not present an increased risk of an RTA in the one study where this has been examined. This class of antidepressant seems to represent a safer choice for the elderly driver. Increased prescribing of SSRIs versus the more problematic TCAs may explain why a recent epiremiological study of elderly drivers (McGwin et al., 2000) stood out in not detecting any significant excess risk for antidepressants as a class. Insufficient is known about the risks associated with other antidepressants to make firm predictions but all appear likely to present a lesser risk than TCAs.

The increasing availability of agents with a lower probability of driving impairment allows the firm recommendation that TCAs should be avoided wherever possible in the older driver. Where their use is indicated, in-depth counselling is warranted and there is sufficient evidence for a recommendation to refrain from driving.

5.10 Antipsychotics

These agents are used to treat psychoses, in particular they are a mainstay of the treatment of schizophrenia. There is comment in the literature that people suffering from schizophrenia may have an impaired ability to drive safely as a result of their illness (Gerhard & Hobi, 1984) and some suggestion that psychomotor performance is improved in such individuals during treatment with antipsychotic medication. (Judd, L.L. 1985), although studies examining increased accident risk among psychiatric patients have not found an increase for schizophrenic patients (see section 4.2.5.3). Most antipsychotic agents, both 'typical' and some 'atypical', have sedative as well as anticholinergic effects by virtue of their antagonistic effects on muscarinic (AchM) and Histamine (H_1) receptors (Brody et al., 1998). The subsequent effect on driving ability is discussed in sections 5.4 and 5.5, where anticholinergics and antihistamines are considered in detail. In addition, 'typical' antipsychotics produce movement disorders through blockade of D_2 receptors in the nigrostriatal pathway (Brody et al., 1998) which, if not well controlled with additional anticholinergic medication, may further impair driving ability. Wylie, Thompson and Wildgust (1993) found a significant decrement in driving performance in patients maintained on depot antipsychotics compared with a control group, which they conclude could be due to the illness, the medication or a combination of both. Grabe et al., (1999) compared the driving ability of subjects prescribed 'typical' antipsychotics with that of a group maintained on clozapine. Driving ability was impaired equally in both groups.

Antipsychotics have not been included in any of the epidemiological studies due to the low numbers of people prescribed them. However, it should be borne in mind that the newer 'atypical' agents are sometimes prescribed to treat anxiety and agitation in the elderly population.

5.11 Antihistamines (H_2 antagonists)

No warning label or caution with respect to driving is advised by the BNF, however, there is the statement that the elderly may be more susceptible to the side effects of this group of medicines, notably confusion and hallucinations.

These agents are all used to heal and to provide prophylaxis for gastric and duodenal ulcers. While both cimetidine and ranitidine are available over-the-counter, all of the medicines in this class are commonly supplied on prescription and are generally subject to close supervised use. Cimetidine, the oldest, has the ability to inhibit the metabolism of many centrally acting depressants, increasing their plasma levels. This may pose traffic safety problems (Starmer 1985), which could be significant in the elderly due to the high risk of polypharmacy in this population.

An additional risk may be present in the elderly person who indulges in social drinking while taking an H_2 antagonist. Gastric first pass metabolism of alcohol, by gastric alcohol dehydrogenase, normally acts as a barrier to toxic blood alcohol levels. Fasting, female gender, old age, dilution of alcohol beverages, chronic alcohol consumption, among others, are all factors which can decrease the gastric metabolism of alcohol. Aspirin and some histamine H_2 antagonists have been shown to increase blood alcohol levels by inhibiting this gastric activity and this may result in unexpected impairment in the performance of complex tasks such as driving (Baraona et al., 1994). This effect of cimetidine was confirmed in a study involving fifteen subjects all with substantial gastric first pass metabolism (Gupta et al., 1995). Their alcohol levels increased with repeated doses with a mean peak of 27 +/– 3mg/dl before and 39 +/– 5mg/dl after cimetidine (P< 0.01). The effect was much greater and longer than after a single alcohol dose. In five subjects who had only minimal gastric first pass metabolism, cimetidine did not have this effect. The authors conclude that under conditions that mimic social drinking, cimetidine increases blood alcohol levels to concentrations known to impair psychomotor skills and these levels persist over prolonged periods of time. A similar effect has been shown with ranitidine (Arora et al., 2000).

5.12 Opiates and opioids

Opiates as analgesics and antidiarrhoeal remedies are frequently prescribed for and taken by the elderly. Sedation is a common side effect and the BNF advises they be labelled with the necessary cautionary wording with respect to driving. One study reports an increased crash risk for older drivers using of opiate analgesics (Leveille et al., 1994) while another from Belgium demonstrated that even patients on high intrathecal morphine dose schedules never reached the maximum legal blood concentration of 20mg/ml (Van den Bosch et al., 2001).

Morphine is a well-known sedative but experimental studies on cancer patients have shown that long-term treatment with morphine does not increase the risk of road accidents (Vainio et al., 1995). It has even been reported that the performance of perceptual and cognitive tasks improved although sedation was increased during treatment for severe malignant pain with sustained release morphine (Lorenz et al., 1997). The authors concluded that this improvement was probably due to the removal of pain as a mental stressor.

5.13 Cardiac drugs

Digoxin, beta-blockers, ACE inhibitors, antihypertensives, anticoagulants.

Central nervous system symptoms may be the first and only manifestation of digoxin toxicity and are most common in the elderly (Cooke 1993). This may have implications for an elderly driver prescribed digoxin. Similarly, although most patients taking beta-adrenergic blocking agents do not normally have adverse cognitive effects (Dimsdale et al. 1989), chronic cognitive impairment and pseudodementia have both been reported in individual patients taking such medication (Rogers & Bowman 1990: Fisher 1992) including the topical use of timolol as eye drops (Nygaard & Hovding 1997). Conversely, there are studies which show improved attention associated with greater resistance to distraction with

beta-blockers (Stein & Strickland 1998). This is most likely to be a function of their anxiolytic properties and may in fact improve the performance of the elderly driver. ACE inhibitors, commonly prescribed as antihypertensives for the elderly, seem unlikely to adversely affect cognitive function and in fact their use may result in a small advantage for psychomotor speed (Stein & Strickland 1998). Methyldopa has also been reported to cause impaired mental function (Paykel et al., 1982).

In contrast to these predictions, the 'Alabama' study (McGwin et al., 2000) found that ACE inhibitors (OR 1.6) and beta-blockers (OR 1.4) significantly increased the risk of 'at-fault' crash involvement in the elderly. Interestingly these medications were also overrepresented in drivers assessed as 'not at fault' (OR 1.4 and 1.6 respectively), compared with the control group of drivers not involved in crashes. Heart disease was associated with an increased crash-risk in at-fault drivers only (OR 1.5) as was stroke (OR 1.9). Importantly, both ACE inhibitors and heart disease/stroke remained significant independent risks when each was adjusted for the effects of the other. A similar relationship was found for the presence of anticoagulants (at fault OR 2.6, adjusted for heart disease and stroke OR 1.9). This is the first study to have examined these risks (McGwin et al., 2000) but, as pointed out above, it requires confirmation. The authors speculate that side effects of ACE inhibitors such as vertigo, dizziness, hypotension and syncope could play a role in generating the excess risk. It is important that these are typical signs of over-medication that apply to antihypertensive agents in general (BNF). However, the excess risk of the use of ACE inhibitors appeared to be confined to patients also taking NSAIDs (OR 3.4). This is surprising since it is well-known that NSAIDs reduce the antihypertensive effects of ACE inhibitors (BNF) and the authors themselves point out the limited power of these comparisons.

Calcium channel blockers and vasodilators were associated with a decreased crash risk in elderly drivers in the Alabama study (McGwin et al., 2000). The reason for this apparent beneficial effect is unknown and it stands in need of confirmation. In the same study, diuretics were not associated with any increase in risk.

Overview

Despite the relatively benign profile suggested by the small number of experimental studies available, a recent epidemiological study has indicated that ACE inhibitors, beta-blockers and anticoagulants may present an excess risk of an RTA in older drivers. This risk was independent of that presented by the illness the medications were being used for. NSAIDs may increase the risks associated with ACE inhibitors and patients would be well advised not to take OTC NSAIDs when prescribed ACE inhibitors. Over-medication with antihypertensive agents and digoxin can produce side effects that impair driving and close attention to dose-adjustment is required.

5.14 Corticosteroids

Chronic cognitive deficits in attention, concentration and memory have been reported with corticosteroid therapy (Varney et al., 1980).

5.15 Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

Acute, clinically significant memory and concentration disturbance has been reported in elderly patients taking these analgesics (Goodwin & Regan 1982). It should be remembered that ibuprofen is available over-the-counter without a doctor's prescription and is frequently taken by the elderly for arthritic and rheumatic complaints.

The Alabama study (McGwin et al., 2000) found that use of NSAIDs increased crash risk in both at fault (OR 1.7) and not-at-fault (OR 1.4) elderly drivers with respect to matched controls. Foley et al., (1995) also report NSAIDs as being associated with increased crash risk. The mechanism of such an effect is speculative. The excess risk apparently presented by NSAIDs may be associated with the conditions for which they are used (McGwin et al., 2000, Foley et al., 1995). Against this interpretation, McGwin et al., (2000) found that the risks presented by NSAIDs and arthritis were independent. However, NSAIDs are prescribed for many medical conditions and some are also available OTC, the excess risk apparently presented by NSAIDs may thus represent 'undiagnosed arthitis or other musculoskeletal impairments' (McGwin et al., 2000) in addition to the cognitive effects described above.

Combined use of ACE inhibitors and NSAIDs has been reported to increase crash risk in the elderly (McGwin et al., 2000, see section on Cardiac drugs and antihypertensives).

5.16 Hypoglycaemics

Insulin, oral hypoglycaemics.

Restrictions on driving by medicated diabetic patients are described in section 4.2.6.1, particularly in relation to diabetic control and hypoglycaemia. Symptoms of hypoglycaemia, which include headache, fatigue, impaired concentration, irritability and confusion can produce varying degrees of psychomotor function impairment (Walter 1990). Experimental studies have associated hypoglycaemia with impaired cognition (De Foe et al.,1988) and memory (Stevens et al.,1989) as well as decreased performance in tests on vision, information processing and motor coordination (Hoffman et al.,1989: Stevens et al., 1989) Older patients especially may develop such symptoms without warning (Mori & Ito 1988).

The risk of hypoglycaemia as a result of taking oral sulphonylurea hypoglycaemic agents, is less than that with insulin. However, it can be a complication of therapy and the risk increases with age. It may also occur as a result of drug interaction. This may be significant for the older diabetic driver.

In the Alabama study, use of insulin did not appear to increase crash risk in older patients (OR 0.9) while oral hypoglycaemic use resulted in an excess risk (OR 1.3) in 'at-fault' drivers only.

5.17 Anticonvulsants

Phenobarbitone, phenytoin, carbamazepine, valproate.

Phenobarbitone is sedative and causes dose-dependent impairment of intelligence test performance, vigilance, memory and psychomotor functioning. (Stein & Strickland 1998). The BNF cautionary labelling regarding driving is required with phenobarbitone but not with phenytoin or carbamazepine which cause less severe, but still dose dependent impairment in this respect. Carbamazepine causes the least cognitive deficit but in a study which considered road tracking and car following in actual traffic, carbamazepine produced mild but still sufficient impairment to put epileptic patients at risk while driving at least during the initiation of therapy (Ramackers et al., 2002). It should be remembered that carbamazepine is often prescribed as a mood stabiliser as well as an anti-epileptic.

6 General Conclusions

This document has demonstrated that more older people are driving, they are driving more and are expecting to continue to do so more than ever before. In particular, it is those groups who have traditionally been less likely to drive who are increasing their driving, that is, the very old and older women. Physicians can now rarely assume that any patient does not drive. The need for improved knowledge of patients' driving status and updated training for doctors on the driving restrictions relating to different illnesses has been discussed. Importantly, the document has emphasised the need to help older drivers maintain safe driving, rather than encouraging them to give up except in circumstances where assistance to improve safety and ease of driving is unlikely to successfully reduce their risk. It is acknowledged that older people are at higher risk as pedestrians than as drivers.

Many categories of illness and different classes of medication have been considered in detail, and the emphasis has been placed on the importance of actual function. This is an approach clearly indicated by the literature in many areas – simple diagnosis of an illness or prescription of a particular class of medication is often a poor predictor of actual accident risk and individually varying factors such as effects of other illnesses or medication, extent of normal age-related declines in functions such as vision, speed of processing or motor abilities all need to be considered. In many cases, an otherwise unimpaired person can compensate successfully for mild deficits induced by some medication or impairments, especially if they are aware of such deficits. Some studies have demonstrated that although risk for a particular illness may be generally found to be high, the fact that patients are able to reduce their risk by adapting their driving in some way results in no increased risk for that group.

Although older people have generally been found to be well motivated to reduce their risk when aware that they are at increased risk, there is evidence to suggest that such self-awareness reduces in accuracy with increasing age and particularly with increasing cognitive impairment. This suggests that advice on any increased risk is valuable.

Nevertheless, there is significant evidence that some illnesses and medication have serious effects on driving. Changes in metabolism that accompany old age, together with an increased sensitivity to side effects, particularly to those on the central nervous system, suggest that this is a particular difficulty for people as they get older.

7 References

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