J. Roy. Coll. Phycns Vol. 12 No. 3 April 1978

Risks at Work from Medication

FELICITY EDWARDS, DM, MRCP

Senior Employment Medical Adviser, Health and Safety Executive, Employment Medical Advisory Service, Birmingham

The Health and Safety at Work Act (1974) has engendered awareness, both inside and outside industry and in the professional press and the national media, of the many problems related to the maintenance and improvement of safety standards. Most attention has naturally been paid to the hazards inherent in some work situations, particularly to the undesirable effects on health of exposure at work to certain environmental conditions and any consequent morbidity and mortality. We can regard the worker as exposed to 'external pollution' in this respect: although any adverse effects of exposure to such substances are the result of their introduction into the body, both exposure and intake are involuntary.

The other side of the coin concerns the possible effects of the worker's own health on his performance and consequent safety at work. One aspect of this is the risks at work from medication: this includes medicines prescribed by doctors and those available over the counter. The term 'drug' is used for these medicines but the drugs of addiction and abuse are not discussed. The voluntary introduction into the internal environment of chemicals, usually in the form of medication, and particularly their unnecessary consumption has been called 'internal pollution' (Warburton, 1977).

The field on which I shall concentrate is that of certain psychotropic drugs, including those widely prescribed at the present time. These are the hypnotics, sedatives and minor tranquillisers which have broadly similar effects. In addition, I shall touch on the antihistamines which are the only compounds I shall mention that are available for self-medication in Great Britain. Alcohol, the most popular psychotropic 'drug', will be mentioned only in its relations with other medication. Other therapies, such as those used for controlling blood pressure, are still being evaluated, and will not be discussed.

The responsibility for any hazard at work related to the consumption of medication lies with two groups: first, on the medical profession which prescribes, and, secondly, the pharmaceutical industry which prepares the compounds. Data sheets on medication are provided for prescribers by the manufacturers and all adverse effects should be included; some information should also be available when products are bought over the counter.

Information on any possible adverse effect should be transmitted to the patient, and the medical profession, which bears the responsibility for writing a

prescription, should take the precaution of checking on the nature of the patient's work and give adequate warning both on any relevant adverse effects and on the correct way to take the tablets prescribed, making sure the patient understands this advice. This is especially important when medication is taken for the first time. Doctors should also assume that most of their adult patients drive a motor vehicle; with 21 million private driving licences in Great Britain this is much more likely than not.

Patients should be alerted to the fact that some medicines, though necessary, do have undesirable effects that might affect safety, and should maintain the right to ask their doctors about this and to inform their employers if it is appropriate. Management have a responsibility for safety at work and should be alerted by employees and/or occupational health staff to any potential hazard to the individual worker or to others, from a given individual's medication if he is working in hazardous situations, which may possibly contribute to accidents or near accident situations. The Post Office is taking a lead in this field.

However, it would be naïve and simplistic to attempt to devise a risk benefit formula applicable to all medication, with a zero on the risk side of every equation: and if there is a slight risk, which is likely to be unquantifiable, we must never discount the potential benefits. Indeed, in certain cases the medications I shall discuss later, where their use is clinically necessary, may be keeping some people at work more safely than they might be without their therapy. 'We engage in an unbalanced science that quantifies risk and not benefit' (Feinstein, 1972) and have to apply what has been described as 'an empiric but balanced scheme of assessment that is sometimes called common sense'.

Therefore we must first consider the problem in relation to the *raison d'être* of the medication, that is, the primary illness. The majority of people have an illness needing some definitive treatment at some stage in their working life and I must emphasise that, in most instances, the patient who needs a specific treatment will, if at work, be safer with it than without. Many serious chronic illnesses for which regular maintenance treatment is needed, such as substitution treatment for endocrine disorders or pernicious anaemia, are examples of necessary treatment which has to continue to maintain an active working life. Two major illnesses come into this category: diabetes mellitus and the epilepsies. The majority of diabetics are working well within the limits of their own safety. However, those on insulin treatment may not always be able to undertake work where restrictions leading to isolation in space and/or time are a necessary part of that occupation. Epilepsy is perfectly adequately controlled in very large numbers of those afflicted and many work situations are open to patients whose seizures are controlled in this way. Obviously, medication is necessary for such people to continue at work. But certain occupations will not be possible and, because of the problems associated with adjustment of treatment, shift work is inadvisable.

Whether the patient is fit to work because of the underlying illness is the first

question that must be answered by his own doctor or other medical advisers. This can be summed up by a modified version of the three questions the Civil Aviation Department suggests that pilots taking permitted medication ask themselves before flying (Kelly, 1973) and which I would urge that the medical profession should always remember to ask, when advising those who are at work.

1 Is the patient fit to do his work?
2 Does he really need this medication?
3 Has he noticed any adverse effects, particularly those that may affect safety aspects of working life?

Adverse effects may be due primarily to the active principles of the drug itself in normal doses and may be exaggerated by prolonged repeat prescriptions; for example, drowsiness from daily tranquillisers. Secondly, there are specific 'toxic' adverse drug effects produced by idiosyncratic hypersensitivity or allergic reactions. The third important type of adverse effect is due to the combination of two or more compounds, one of which may be alcohol. The combinations may be additive (as with alcohol and the hypnotics) or may result in one of the drugs being metabolised too rapidly and, hence, failing to achieve its desired therapeutic effect because the other drug is a potent hepatic enzyme inducer. It is the first category of adverse effects that I wish to look at in detail.

My own interest in this subject developed while I was working at an Employment Rehabilitation Centre attempting to assess objectively both the health and the fitness for work of the diverse clientele. Attempts to forecast work potential are naturally difficult but when many of the clientele concerned were regularly receiving either repeated doses of diazepam or other anxiolytic drugs by day or were suffering from the persistent after-effects of regular and often large doses of hypnotics taken each night, it became problematic. Slowness of reaction, lack of attention, and poor motor co-ordination could have existed before treatment and might be worse after treatment ends but these combined with a lack of subjective awareness of impaired performance made one suspicious of drug effects; relatives occasionally provided a clue. Performance in the Centre workshops and performance as judged by the occupational psychologist's tests could both be affected.

Doctors often assess the effectiveness of treatment by looking at 'hard' or quantifiable data, while other 'soft' data, such as effects on daily life and its convenience, are rarely taken into account (Feinstein, 1972). Yet effects on performance may be measurable in an experimental situation and the measurements may well be applicable by inference to the therapeutic situation. There is little information on the possible role of perceptual or motor defects or disturbances in the man and their effect on the machine. Such defects may be permanent or transient and, if transient, may be related to the taking of medication. We wish to alert colleagues to these possible hazards.

In the last few years, since the beginning of the 'benzodiazepine bonanza' (Tyrer, 1974), increasing attention has been given to the immediate and delayed effects that this class of drugs has on performance, particularly on skilled performance. Observations on the barbiturates in the 1950s had indicated that measurable effects, including impairment of attention, visual perception and ability to compute, continued for some hours after administration. Over the last 10 to 15 years the previously widespread use of barbiturates by prescribers has steadily declined because of their particular attributes related to tolerance and addiction, and their power as central nervous system depressants which made them an effective method of suicide.

Henry Miller, writing in 1973, thought that the area of psychotropic drugs was 'the most important growing point in therapeutics' at that time. The treatment of the schizophrenias with the major tranquillisers and of the depressive illnesses with antidepressants has resulted in more effective treatment and greater control of therapy. The use of the major tranquillisers and antidepressants has ensured that many people with chronic psychoses are now able to live a much more normal life in the open community. However, many physicians feel that the benefits of the minor tranquillisers and the risks of their excessive use should be questioned (Dunlop, 1970; *Lancet,* 1973; Parish, 1974).

It is clear that many patients continue to receive repeat prescriptions from their doctors (Wade, 1977), and there is evidence that some hypnotics, sedatives and minor tranquillisers are over-prescribed at present (*British Medical Journal,* 1974; Dunea, 1977; Howie, 1977). Dunnell and Cartwright (1972) surveyed a sample of the adult population in Great Britain for two weeks in 1968. They found that 5 per cent of all medicines were sedatives, sleeping pills or tranquillisers, the fifth largest group of medicines, after analgesics, laxatives, antacids and nutritional supplements, all of which of course can be bought over the counter. One-fifth of all prescribed medicines acted on the central nervous system and in only one in five of such instances could the patient recall being advised about adverse effects, or the dangers of driving, or the dangers of taking alcohol. A quarter of the medicines prescribed a year or more before were for the central nervous system (mainly tranquillisers, sedatives and hypnotics) and one in 12 adults had taken such drugs for one year or more. One in five of all prescriptions had been repeated 40 times. It is probable that many repeat prescriptions are not medically necessary and it is obvious that the onus of adjusting or terminating treatment should in most instances be on the doctor, not the patient. Prescriptions by family doctors account for over 90 per cent of the cost of pharmaceuticals; the hospital sector of the NHS contributes less than one-tenth of the total drug bill (Wade, 1977).

The background to the present level of prescription of such drugs is one of a steadily increasing number of prescriptions of non-barbiturate hypnotics, together with a steady increase in the prescription of such compounds for use by day as

Table 1. Number of prescriptions in millions – England and Wales (Office of Health Economics, 1977).

	1965	1966	1967	1968	1969	1970	1971	1972	1973	1974
Hypnotics (barbiturate)	17.2	16.8	16.1	15.3	13.1	12.2	11.7	10.5	9.6	8.6
Hypnotics (non-barbiturate)	2.7	3.5	4.8	5.8	5.9	6.6	7.7	8.4	8.8	9.5
Tranquillisers	10.9	12.5	14.7	16.0	15.4	16.0	18.4	19.5	20.6	21.5

tranquillising agents, with a steady decline in barbiturate prescriptions (Office of Health Economics, 1977) (Table 1). The increase has been mainly in the minor, rather than the major tranquillisers (Blackwell, 1969). For England and Wales the total number of prescriptions rose from 30 million in 1965 to 40 million in 1974. This figure includes barbiturate and non-barbiturate hypnotics, but if the barbiturates are excluded the figures rise from 14 million to 31 million over the ten-year period.

Table 2 shows the percentage of different age groups, for each sex separately, who had consumed anti-anxiety compounds and/or sedatives in the previous year in the UK. The same survey also showed that in the UK 5 per cent of men and 12 per cent of women (8.5 per cent of all persons) had consumed these drugs on a daily basis for one month or more during the previous year and that the position was similar in other countries (Balter *et al.*, 1974). A recent survey in Germany of 2,000 people aged 50 showed that 15 per cent of men and 27 per cent of women were regular and recent users of tranquillisers (Pflanz *et al.*, 1977).

The main advantages of the benzodiazepines over the barbiturates are safety, even in very large doses, and rare physical dependency; and as they are not hepatic enzyme inducers at the dose normally prescribed, they do not interfere with other drug treatment. However, some of their disadvantages are as follows: they may cause drowsiness and confusion and in many cases lead to measurable residual effects on skilled performance; they add to the effects of other central nervous

Table 2. Percentage of each sex/age group using anxiolytics/sedatives in 1971 in UK (Balter *et al.*, 1974).

Age	16-24	25-34	35-44	45-54	55 +		
Males	4.5	3.1	9.2	9.6	13.9	All Males	8.9
Females	17.2	20.1	15.6	23.6	18.6	All Females	19.1
						All Persons	14.2

system depressants such as alcohol; they may occasionally produce psychological dependency, and in some instances they can lead to unpredictable aggressive behaviour. It is the first two of these disadvantages that are relevant to possible risks at work.

Studies of the immediate and residual effect of diazepam on performance have used various tests which fall into six main categories, including ability to sustain concentration, or attention and vigilance; decision making; learning and memory; psychomotor performance and perceptual motor skills and reflex speed. In all these tests, with the exception of simple reflex response, impaired performance has been shown after intake of therapeutic doses of diazepam (Kleinknecht and Donaldson, 1975). Because such motor skills relating to co-ordination are important in the context of driving and because alcohol is well known as one of the most important drugs affecting all these types of skills, the authors suggested that the interaction of these two substances has great importance. They also emphasised that subjects taking diazepam were unaware of their own impairment of performance, and that alcohol and diazepam taken together resulted in decrements greater than when either drug was taken alone. With respect to driving, a lack of awareness of one's own impairment may be especially hazardous. One of the 'virtues' of the barbiturates was that the hangover effect produced by them was such that the subject was often aware that he was, in fact, still under the influence of a drug, but this is not the case with many of the benzodiazepines.

Nicholson (1976) has reviewed the residual effects of hypnotics and discussed their implications outside the world of aviation medicine in which his own work was done. Hypnotics have been looked at within the therapeutic range of doses and some have been shown to impair performance significantly during the day after a sleep-inducing dose at night. Nicholson emphasised that the type of skills tested and shown to be impaired in these studies, which have led to a ban on most hypnotics for pilots, are likely also to be affected in other skilled work. The work of Nicholson and his group, using mainly tests of visuo-motor co-ordination, has shown that the effects of diazepam are short-lived and that, if it is used as a hypnotic at night, by the time the subject is awake and at work the following morning any residual impairment will have disappeared and the subject's performance will have returned to its normal level. This is not the case with one of the most commonly used hypnotics in Britain – nitrazepam, which causes a marked reduction of performance that persists throughout the whole of the subsequent day (Nicholson, 1976).

Bond and Lader (1972) reached similar conclusions on the residual effects of hypnotics and confirmed that lack of awareness of impaired performance after nitrazepam at night may persist, even when the impairment is obvious. The ability to perform simple repetitive motor tasks was most impaired, and reaction time was increased. They felt it essential that people taking therapeutic doses of hypnotics should be warned of the likely residual effects. The effects of occasional

sleep deprivation have been shown to impair subsequent performance less than the effects of standard hypnotics.

Dunlop (1970) has estimated that approximately one night's sleep in every ten in the UK is hypnotic-induced. If this is so, many unsuspecting people are living and working, in addition to sleeping, under the influence of an hypnotic with persistent effects, such as nitrazepam, and might well perform better without it. However, when sleep is a problem, and particularly where it may be related to the nature of the work involved (for aircrews in long distance flights, for some shift workers and those working at night) hypnotics may be essential for enough rest. Those without residual effects on performance, such as diazepam, would seem to be the treatment of choice.

It is important in future evaluation of drug effects on performance to look at differences between groups and between subjects, as there is great variation in response to psychotropic drugs (Sambrooks *et al.*, 1972). Doctors should bear this in mind when prescribing and should review prescriptions, when seeing patients, so that a hypnotic is selected for the individual which will suit him and his occupation. Tyrer (1977) recommended that the initial prescription should be for two weeks or less and that the reason for the prescription should be reviewed whenever the patient was seen again.

Changes in an individual's reaction times after hypnotics have been shown to be related to plasma level. Increasing doses were related to rising plasma concentration of the drugs concerned and to changes in reaction time, and a relationship was shown between the peak plasma concentration and the overall effect of the drug (Curry *et al.*, 1977). Great individual variation occurs with the same drug. The blood level of diazepam after a standard dose given to 29 subjects varied by a factor of more than 20, after a given time interval (Garratini *et al.*, 1973). These different levels may be important, as they correlate with the degree of drowsiness, at any rate after one dose, shown by the subjects. If dosage is repeated it has been shown that, with a daily dose of nordiazepam (one of the main metabolites of the benzodiazepines) taken as clorazepate for 14 consecutive days, the plasma concentration varied considerably between the six subjects studied and also that, after treatment ceased, plasma levels took several days to return to pre-treatment levels (Curry, 1977).

Although usually taken over a much shorter period of time than many of these psychotropic compounds, antihistamines induce drowsiness and inattention. They are known to be central nervous system depressants and have been shown to produce significant impairment of hand/eye co-ordination in normal people, probably by a direct central effect (Large *et al.*, 1971). Most of these products for sale over the counter are now marked as potentially hazardous when used in relation to driving and work on heavy machinery. The antihistamines are widely distributed in various 'cold cures' and in anti-travel sickness compounds, and their adverse effects are increased by alcohol. It is important that this should be made

known to patients if antihistamines are prescribed, and if they are bought over the counter this should be indicated on the packet.

Two specific accidents illustrate the possible contributory role of medication. First, in the investigation of a fatal aircraft accident a combination of medicines and other preparations was found in the personal effects of a very experienced pilot who, by stalling his small monoplane, was killed together with one of his two passengers (Underwood Ground, 1975). Apart from three unbroken bottles of whisky, one of which had been opened, other items found included a hip flask (containing a very small amount of whisky) and other compounds as follows: numbers of capsules of chlordiazepoxide (one of the first benzodiazepines to be introduced); an inhalant for asthma containing adrenaline, atropine and papaverine; a large bottle of mist. Kaolin and Morph.; an anti-amoebic compound; a half empty tube of Alka Seltzer; codeine tablets, vitamin B1 compound, and antihistamines – cyclizine (Marzine). The conclusion was that in this accident alcohol was the primary contributory factor but in the report the additive effects which the benzodiazepine and/or antihistamine might have had were emphasised. No pilots are, of course, allowed to fly if they are taking hypnotics, although some relaxation with regard to this rule has recently occurred. Because of its very short effect on performance, diazepam is allowed in single doses of 10 mg or less, only for inducing sleep (Nicholson 1977).

Diazepam was referred to in a report of a railway accident in Scotland in 1974. The driver of the train had recently been prescribed diazepam by his own doctor. The expert to whom the case was referred stated that in work such as that of a train driver on a familiar route, reaction to different stimuli would occur with a minimum of attention: if the level of attention had been depressed by the sedative effect of a drug, speed of reaction to a potentially dangerous situation could be reduced. The report recommended advising staff whose duties were concerned with train movements, or who worked near rail tracks, to ensure that their doctors were fully informed of their occupation when any prescription was given and that advice could also be obtained from occupational health staff of British Rail, and that the British Railways Board should bring to the notice of all staff certain medications 'which might impair the proper performance of their duties' (Department of the Environment, 1975).

In the latest edition of *Medical Aspects of Fitness to Drive,* studies on drugs and driving were summarised in 1976. In one study reported, four per cent of a large number of drivers regarded as having been at fault in just over 2,000 accidents occurring over a four year period in Britain were judged to have had their driving impaired by drugs other than alcohol (Havard, 1976). The Blennerhassett Committee considered that, although drugs accounted for perhaps only 100 cases detected each year as compared with over 50,000 related to drinking, impairment of driving skills from medication was likely to be underestimated because it is so difficult to obtain proof of consumption of drugs compared with alcohol (Depart-

ment of the Environment, 1976). In this context, professional drivers and private drivers are rather different, and I must emphasise again that in very many cases people will be driving more safely with their therapies than without. But a doctor must think very carefully when prescribing hypnotics, sedatives or tranquillisers for a professional driver, and special attention should be paid to the dangers of unwanted interaction with other drugs, especially alcohol. Silverstone (1977) has emphasised that, as between three and five per cent of drivers are taking psychotropic drugs at any given time, and as over half these drugs are likely to be minor tranquillisers, there is a considerable number of drivers at risk from possible adverse effects of such drugs on related motor skills. He felt that benzodiazepines were a potential hazard because they impaired psychomotor function and might affect both judgement and car handling. However, he also strongly emphasised that further epidemiological studies with controls were badly needed.

Evidence has been produced of both the 'laboratory' and 'epidemiological' type showing that diazepam was a 'significant although relatively minor causative factor' in some serious road traffic accidents in Norway: there was a considerably greater prevalence of drivers in the accident group with evidence of diazepam and/or alcohol in their blood than in the control group examined (Bø *et al.*, 1975). Because it included a 'control' group (although not perfectly matched), which is rare, and related to the driving situation, it is an important study. In the field of road traffic accident studies the importance of alcohol *per se* is well known but it has extra importance because it enhances other central nervous system depressants. All patients on such medication must be told by their prescribing doctor that alcohol will exaggerate any side effects, and, if bought over the counter, this should be clearly marked on the preparation.

Can it be assumed that there are instances when accidents might not have happened but for the intake of certain medication? These may not be numerous but, as they are not overt, it is impossible at present to assess their significance in relation to the type of accident or injury, or the nature and type of the industry concerned. Medication has probably contributed to some driving accidents, and may therefore be regarded as a potential contributory cause of other accidents until further evidence is available. Can evidence collected in experimental conditions be extrapolated to the 'real life' situation of either driving or work? Further and more adequate data must be collected before such assumptions can be validated; however, by bearing in mind the possible association between medication and/or alcohol and accidents, a primary concern with the prevention of accidents can be stressed.

In conclusion, there is a steadily increasing number of prescriptions for minor tranquillisers and hypnotics. Together with evidence relating to repeat prescribing, it seems likely that many people of working age are consuming these medicines at some stage of their working life, probably unnecessarily in some cases. There is a great deal of experimental evidence that the consumption of these drugs results in

both immediate and residual impairment of performance of tasks related to those in skilled and other work. There is some epidemiological evidence that consumption of these medications, particularly in association with alcohol, can be associated with greater liability to road traffic accidents. Although neither of these types of evidence is yet entirely satisfactory, it seems reasonable to suppose that these psychotropic compounds might be contributory factors to some accidents at work. There are as yet no reliable data on the relation of such medication to occupational accidents and thought is being given to possible ways in which this field might be studied. However, the onus lies clearly on doctors prescribing such medication to enquire into their patients' occupation, to indicate possible adverse effects and to supervise the continued use of such compounds, and on pharmaceutical companies to ensure that products available over the counter, which include antihistamines or other compounds with similar effects, are clearly labelled with appropriate warnings. A recent collection of essays from America, critically examining some of the problems of health care systems in an affluent society, is entitled *Doing Better and Feeling Worse* (Knowles, 1977). I suggest that, with the increasingly widespread, and perhaps uncritical use of some psychotropic medicines, many working men and women will be feeling better, but doing worse, and that this might result in risks to safety, the responsibility for which rests basically on the medical profession.

Acknowledgements

I would like to acknowledge the help and advice of Professor Owen Wade, Professor of Therapeutics, University of Birmingham, Group-Captain A.J.C. Balfour, RAF Institute of Pathology and Tropical Medicine, Wing Commander A. N. Nicholson, RAF Institute of Aviation Medicine, Dr Andrew Raffle, Chief Medical Officer, London Transport Executive and Dr Peter Taylor, Chief Medical Officer, Post Office.

This article is based on a paper read at the symposium on Assessment of Health Risks at Work held in the Royal College of Physicians in November 1977.

References

Balter, M. B., Levine, J. and Manheimer, D. I. (1974) *New England Journal of Medicine,* **290**, 769.

Blackwell, B. (1969) *Prescriber's Journal,* **9**, 29.

Bø, O., Haffner, J. F. W., Langard, Ø., Trumpy, J. H., Bredesen, J. E. and Lunde, P. K. M. (1975) *Proceedings of the Sixth International Conference on Alcohol, Drugs and Traffic Safety* (Ed. Israelstam and Lambert). Toronto: Addiction Research Foundation.

Bond, A. J. and Lader, M. H. (1972) *Psychopharmacologia,* **25**, 117.

British Medical Journal (1974) **3**, 300.

Curry, S. H. (1977) *Drug Disposition and Pharmacokinetics* (2nd ed). Oxford: Blackwell Scientific Publications.

Curry, S. H., Whelpton, R. and Scott, D. F. (1977) *British Journal of Clinical Pharmacology* **4**, 109.

Department of the Environment (1975) *Report of a Railway Accident in 1974.* London: HMSO.
Department of the Environment (1976) *Drinking and Driving – Report of the departmental committee.* London: HMSO.
Dunea, G. (1977) *British Medical Journal,* **3,** 240.
Dunlop, D. (1970) *Proceedings of the Royal Society of Medicine,* **63,** 1279.
Dunnell, K. and Cartwright, A. (1972) *Medicine Takers, Prescribers and Hoarders.* London and Boston: Routledge and Kegan Paul.
Feinstein, A. R. (1972) *Lancet,* **3,** 421.
Garratini, S., Mussini, E. and Randall, L. O. (Ed.) (1973) *The Benzodiazepines.* New York: Raven Press.
Havard, J. D. J. (1976) In *Medical Aspects of Fitness to Drive* (Ed P. A. B. Raffle). London: Medical Commission on Accident Prevention.
Howie, J. G. R. (1977) *Prescriber's Journal,* **17,** 58.
Kelly, H. B. (1973) Advisory Group for Aerospace Research and Development (AGARD) Conference Proceedings no 108, on the use of medication and drugs in flying personnel.
Kleinknecht, R. A. and Donaldson, D. (1975) *Journal of Nervous and Mental Disease,* **161,** 399.
Knowles, J. H. (Ed.) (1977) *Doing Better and Feeling Worse.* New York: Norton and Co. Inc.
Lancet (1973) **2,** 1101.
Large, A. T. W., Wayte, G. and Turner, P. (1971) *Journal of Pharmacy and Pharmacology,* **23,** 134.
Miller, Henry (1973) *Medicine and Society,* London: Oxford University Press.
Nicholson, A. N. (1976) In *Royal College of Physicians Advanced Medicine 12* (Ed. D. K. Peters). London: Pitman Medical.
Nicholson, A. N. (1977) Hypnotics and aircrew (address to the 12th International Symposium of Civil Aviation Medical Association, London).
Office of Health Economics (1977) *Compendium of Health Statistics,* 2nd ed. London: OHE.
Parish, P. A. (1974) *The Price of Tranquillity,* Occasional paper 4. London: MIND.
Pflanz, N., Basler, H.-D. and Schwoon, D. (1977) *Journal of Health and Social Behaviour,* **18,** 194.
Sambrooks, J. E., MacCulloch, M. J., Birtles, C. J. and Smallman, C. (1972) *Acta psychiatrica Scandinavia,* **48,** 443.
Silverstone, J. T. (1977) *Pharmaceutical Journal,* **219,** 309.
Tyrer, P. (1974) *Lancet,* **3,** 709.
Tyrer, P. (1977) *Practitioner,* **219,** 479.
Underwood Ground, K. E. (1975) *Aviation, Space and Environmental Medicine,* **46,** Pt. 10, 1284.
Wade, O. (1977) In *Clinical Practice and Economics* (Ed C. I. Phillips and J. N. Wolfe). London: Pitman Medical.
Warburton, D. M. (1977) Psychology Section, British Association for the Advancement of Science.