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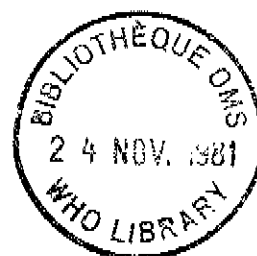
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HEALTH CARE OF THE ELDERLY

Report on the Technical Group on Use of
Medicaments by the Elderly



Thônex

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SUMMARY REPORT

The present meeting is one of a series devoted to specific technical issues concerning the health care of the elderly. The Use of Medicaments by the Elderly was selected as a topic of priority concern by a Committee which met in 1978 to advise the World Health Organization's Regional Office for Europe on a programme of cooperation with Member States designed to advance the wellbeing of elderly citizens. The 3 main objectives of the meeting were those proposed by the 1978 Committee (World Health Organization, 1978), namely: to review existing pharmacological knowledge in relation to old age; to define indications for use of drugs in old persons, and to consider problems of "overdiagnosis", overtreatment and polypharmacy; to provide information on the most useful drugs for use in old patients.

A fourth objective concerning the increased prescription and use of psychotropic drugs in old age is more fully covered in the report of a related WHO-supported meeting, namely the Ninth Symposium on Clinical Pharmacological Education in Drug Control held in Schlangenbad, Federal Republic of Germany on 18-21 November 1980 (World Health Organization, 1981).

The recommendations of the 1978 Committee were followed also with respect to the disciplinary constitution of the group, which included (see Annex 1) a pharmacist and clinical pharmacologists with special interest in old age, specialists in geriatric medicine, a nurse, a primary care physician, a psychiatrist with special interest in geriatric psychiatry, and experimental biologists. The group was supported by global and regional WHO staff in the fields of care of the aged, mental health, pharmaceuticals, drug policies and management, and included a member of the 1978 Advisory Committee.

The full report which follows provides a comprehensive review of drug prescribing for the elderly, describes current knowledge on geriatric clinical pharmacology, considers the issues of self-medication and compliance and makes a brief reference to drug misuse. There then follows a set of principles for promoting rational drug therapy for the elderly, together with a list of drugs usually given in reduced dosage in the elderly. A further list gives drugs with potentially severe or unusual side effects in the elderly and includes a subset of those to be avoided, if possible. Finally, the report concludes with 11 recommendations. Highlights of the Report are summarized below:

1. Prescribing patterns

Where the proportion of elderly (60 years and over) in the population is very high (approximately 20 per cent of total population), 50 per cent or even more of the total drug consumption is by the elderly. Data from published sources which indicate the level of prescribing in different settings are as follows:

In hospital, in Scotland, patients (including the elderly) were reported to be receiving an average of 4.6 drugs

In long-term care institutions, in the United States, patients received a mean of 8 drugs in the first 10 days.

In the community, in Canada, elderly people reported taking a mean of 3.2 drugs.

The group concluded from this review that polypharmacy appeared to be the rule in acute hospitals and in institutions and that psycho-active drugs appeared to be universally used where most of the mentally disabled are found.

However, drug prescribing varies widely and, to allow comparison in drug utilization between or within countries, the methodology of the Defined Daily Dose (DDD) is proposed, a procedure recommended by the WHO sponsored Drug Utilization Research Group.

2. Geriatric clinical pharmacology

The group considered drug distribution and elimination (pharmacokinetics) and drug response (pharmacodynamics).

The elderly differ from the young in the quantity of the drug delivered to the target organ, and possibly in the sensitivity of that organ to the drug. In spite of this, drugs tend to be taken in similar doses by both age groups, and it is not surprising therefore that overdosage occurs more commonly in the elderly. Although such knowledge has been present for a number of years, there are very few drugs for which a specific geriatric dosage is recommended, and dosage regimens for new drugs are still established on data obtained in younger individuals.

2.1 Drug distribution and elimination

No change in the rate or amount of drug absorbed from the gastrointestinal tract has been observed with aging. There is insufficient evidence to draw any general conclusion on the effect of aging on the volume of distribution. Thus the elderly are at risk from relative overdosage of drugs due to inefficient pathways for drug elimination and metabolism. Age-related changes in drug elimination rates are most important in those drugs with a narrow therapeutic index such as digoxin, aminoglycosides and hypoglycaemic agents. In short, impaired elimination of drugs because of diminished renal function or hepatic metabolism is a major cause of the increased incidence of adverse drug reactions in the elderly.

2.2 Drug response

Knowledge of alteration in drug response with aging is at a preliminary stage, but evidence strongly indicates that drugs acting on the central nervous system produce an enhanced response for a given plasma concentration.

3. Self-care and self-medication

It was emphasized that self-medication is only one aspect of self-care, the encouragement of which is of great importance in meeting the demands for health care, both in developed and developing countries. Studies show that self-medication is widespread and also highlight the need for education concerning non-prescription medications.

4. Compliance

Although advanced age, by itself, does not appear to be a significant factor affecting compliance, age-related factors such as polypharmacy, memory and visual impairments do affect its quality. Manifestations of this include failure to take drugs at certain times, interruption of treatment, errors in doses, drug-taking at incorrect intervals and addition of other drugs.

5. Drug Misuse/Abuse in the Elderly

Reference was made to a report which stated that nearly 20 per cent of the patients entering the geriatric service of a general hospital displayed symptoms attributable to the effects of prescription drugs.

6. Strategies for rational drug therapy for the elderly

The most important principle for promoting rational drug therapy for the elderly is the question "Is drug therapy required?", since there is no need to prescribe a drug for every disease or symptom. Also, drug treatment should never be regarded as a substitute for time spent giving the patient helpful advice. It was the experience of the group that many old people admitted to hospital or reviewed during long term hospitalization improved greatly when the regimen of drugs that they had been taking was stopped. However, drugs should not be withheld on account of old age, particularly when appropriate drug treatment can improve the elderly person's quality of life.

The next two principles relate to the number of drugs and the appropriateness of the particular medication in the elderly. Here the prescriber should always order the fewest drugs that the patient needs and he should be aware that certain drugs which are appropriate for treating younger patients may be unsuitable in the elderly, for example, carbenoxolone.

Two principles follow which question the drug to be used, and whether or not the dose needs to be modified. In this case, there is an analogy with paediatric preparations and dosages. Drugs and groups of drugs usually given in reduced (geriatric) doses include aminoglycosides, benzodiazepines, carbamazepine, chlormethiazole, digoxin, haloperidol, levodopa, metoclopramide, pethidine, thioridazine, thyroxine and Vitamin D.

Another list of drugs emerged from questions relating to side effects. Drugs with potentially severe or unusual side effects in the elderly and which should be avoided if possible in the elderly are all barbiturates, bethanidine, carbenoxolone, chlorpropamide, chlorthalidone, debrisoquine, guanethidine, nitrofurantoin, pentazocine, phenylbutazone.

Practical points concerning packaging and labelling and management of self-administration follow. Collaboration with a responsible and interested neighbour or friend is proposed, especially when potent drugs are used.

The final principles concern the assessment of the need to continue medication or indeed of the need to prescribe any drug at all. Many commonly prescribed drugs need not be continued once the acute episode is satisfactorily treated, as for example, with the administration of digoxin in atrial fibrillation complicating pneumonia. Patients should therefore be persuaded to bring their containers to consultations, and to avoid hoarding, since accumulated medicaments can be confusing to the elderly patient.

The recommendations of the group are prefaced by the important statement that aging is not a disease and that, as such, it is not treatable by medicaments. The recommendations relate to the adoption of the standard methodology of the Defined Daily Dose for comparative utilization studies, the extension to other WHO regions of the activities of the European Drug Utilization Research Group, education in geriatric clinical pharmacology and therapeutics for health professionals (including nursing staff and pharmacists in training), use of drug information pharmacists in geriatric medicine, patient education, review of therapeutic regimens, pharmacological research involving elderly patients and healthy elderly volunteers and basic research with aging animal models, drug regulatory requirements needed to generate appropriate drug information for prescriber and patient, health education in self-medication and, finally, research to develop new methods of changing prescribing practice.

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TECHNICAL GROUP ON USE OF MEDICAMENTS BY THE ELDERLY

Although chronological age has been shown to be correlated with response to drugs in certain circumstances, such correlation is not inevitable nor is its nature predictable. At times increasing age seems to predispose to hyperreactivity, at times to hyporeactivity, and at times seems not to affect the magnitude of response in any significant way. It is suggested that the systematic collection of data bearing on this point may provide leads for important contributions to our understanding of the fate and action of drugs. (Lasagna, 1956).

1. DRUG PRESCRIBING FOR THE ELDERLY

1.1 Demographic considerations

In developed countries, trends show that the proportion of elderly in the population has been rising steadily over the past several decades. This is due to a combination of falling birth rate and medical, economic and social factors which favour prolonged life. For example, in the United States, about 11% of the population, more than 23 million people, are now over 65 years of age. It is projected that, by the year 2030, nearly 52 million people will be over age 65 and will constitute up to 17% of the population. According to recent statistics (Gibson et al., 1977), in fiscal year 1976, the aged spent about 25% of the national total of US\$11.2 billion for drugs and drug sundries. On the average, each elderly person spent over \$100 that year for prescribed and non-prescribed drugs. If current trends continue we may expect that by the year 2030 expenditures for drugs by the elderly in the United States may constitute over 40% of the national total. In the United Kingdom, where the elderly represent only 12% of the population, they are responsible for approximately 30% of national health expenditure on drug prescriptions (O'Malley et al., 1976).

Some segments of health care delivery systems in developed countries may bear a disproportionate burden of the health care needs of the aged. Thus, in the United States, the Veterans Administration anticipates that between 1970 and the turn of the century the proportion of adult males aged 65 years or older who are veterans will increase from 26% to 59%. In 1970, there were 2.2 million and by the year 2000 there will be 7.1 million aged veterans who are eligible for care at Veterans Administration Hospitals (National Academy of Sciences, 1977). Such figures emphasize that the needs of geriatric patients will constitute an increasing important aspect of medical care for the future.

1.2 Drug prescribing patterns - hospital

Drug prescribing varies widely in different countries. This has been verified by the Boston Collaborative Drug Surveillance study which was conducted in the United States, Canada, Israel, New Zealand and Scotland (Lawson & Jick, 1976). The study showed that, on average, United States medical hospital inpatients including geriatric patients had received 9.1 drugs compared to 7.1 for Canada, 6.3 for Israel, 5.8 for New Zealand and 4.6 for Scotland.

In addition, drug reactions were three times more prevalent in the United States and Americans were discharged with 2.1 drugs in comparison to 1.3 in Scotland.

1.3 Drug prescribing patterns - community

In 1978, Guttman reported a study of 447 subjects in the community of Washington conducted between February and June 1976. These were chosen at random and were all living in the community. Fifty-three per cent of the population initially approached refused to participate in the study, 14% because of illness, 15% for personal reasons, and 71% did not specify the reasons. The most frequently used classes of medications were cardiovascular drugs comprising 61.3%, sedatives and tranquilizers 16.6%, anti-arthritic preparations 12.1% and gastrointestinal preparations 11.4%. Over-the-counter drugs were used by 69% of this sample, 51.7% using analgesics; vitamins and laxatives were used by 8.1% and 7.1% of this group respectively.

In London, United Kingdom, Law and Chambers, 1976, surveyed the oldest patients (76 years and over) of their practice. Eighty-seven per cent of this population were receiving prescribed drug therapy and 34% were taking three or more different drugs each day. Freeman from Southampton, United Kingdom, 1979, stated that the number of drugs prescribed for the elderly in an urban general practice is related to the number of episodes of illness. More than half of these episodes were managed without drugs or with only one. Cardiovascular and diuretic drugs were used most often followed by analgesic and psychotropic agents. Cape, 1978, in Canada asked a stratified random sample of senior citizens (65 years old and over) about drug taking in the three days prior to the interview. Each person consumed a mean total of 3.2 drugs. It seems important to state that older patients are probably not more avid over-the-counter consumers than other segments of the population (Bush et al., 1976).

In Nordic countries it has been found that the prevalence of chronic illness varies with age, increasing sevenfold from the age group of 15-34 years (9%) to the age group of 65-74 years or over (65-67%), and that men aged 65 years or more consult a physician three to four times more frequently than men of age 15-34 years. For women, the difference is somewhat smaller. The number of days in hospital also shows an increase of similar magnitude with increasing age (Purola et al., 1974). Prescribing of medicines is an essential part of medical care. Therefore, the use of medicines increases with age but much more markedly than do consultations with a physician. In the oldest age group (over 65 years) it has been found that more than ten times more prescription medicines are used than in the age group 15-35 years (Kohn et al, 1976). The same increase can be seen in the use of non-prescription medicines (in self-medication).

The prescribed doses of drugs usually decline with age. In the county of Jämtland in Sweden the mean prescribed daily dose of amitriptyline decreased from 70 mg in the 15-59 age group to 45 mg at 70 years and, similarly, propranolol from 151 mg to 70-100 mg. The digoxin dose decreased with age slightly from 0.23 to 0.20 mg, as was the case with nitrofurantoin and trimethoprim-sulpha methoxazole (Boethius, 1977). This study used the classification system (Nord. Stat. Med., 1979) and the methodology recommended by the Drug Utilization Research Group sponsored by the WHO Regional Office for Europe for comparing drug usage in different regions and different countries. (World Health Organization, Regional Office for Europe, 1979). This involves the concept of the Defined Daily Dose.

As the number of prescriptions per individual increases with age, so the cost also shows a maximum in older age. The number of people aged 60 years or over varies in the population of different countries from 12 to 21 per cent. This may mean that at least 50 per cent or even more of the total drug consumption is by the elderly.

1.4 Drug prescribing patterns - long term care institutions

Many studies have been published on prescribing for chronic diseases in long term care facilities (Borda et al, 1967; Cooper et al, 1978; Howard et al, 1977; Ingman et al., 1975; and in two Boston long term care facilities the patients hospitalized received a mean of 8 drugs in the first 10 days. In another survey Kalchthaler et al, 1977, investigated the incidence of polypharmacy in a 200 bed long term care facility. Psychotropic drugs were shown to be the most commonly prescribed (61% of the patients), followed by diuretics and anti-hypertensive drugs (46%), anti-microbials (14%), and cardiotonic agents (14%).

Howard et al, 1977, studied the abuse of "as needed" (prn) orders for indications such as antibiotics for fever or diuretics for shortness of breath. He pointed out the economies made by more rational use of "prn" orders (Howard et al, 1978). The contribution of the pharmacist to rational drug usage in long term care facilities has been highlighted by Cooper et al, 1978, who showed that in a year, scheduled drugs were reduced by 19.4% and "prn" orders by 45.9%, the overall reduction going from 7.22 to 4.78 drugs per patient. It is noteworthy that psycho-active drugs (Ingman et al, 1975) were more often prescribed to patients with superior mentation and minimal physical disabilities than to those who were more severely disabled.

A study of a sample of 731 individuals living in long term care facilities in London, Canada, showed that two-thirds were having three drugs or more on a regular basis (Cape, 1978). The investigation stated that similar patterns of drug consumption are found in Europe and Australia.

Polypharmacy appears to be therefore the rule in institutions and acute hospitals, and psycho-active drugs are used universally where most of the mentally disabled are found.

2. GERIATRIC CLINICAL PHARMACOLOGY

Important and sometimes subtle physiological and psychological changes occur with "normal" aging, independent of the more overt diseases which are prevalent in the elderly. These changes might reasonably be expected to alter drug responsiveness as a result of changes in disposition and particularly elimination of drugs and/or changes in organ or receptor sensitivity. It is generally acknowledged that older patients are more susceptible to both the therapeutic and toxic effects of many drugs (e.g. O'Malley et al., 1976). At the present time, only a few drugs have been carefully studied in the elderly and except for drugs predominantly excreted by the kidney it is not yet possible to generalise on the type or magnitude of changes. While most pharmacokinetic studies in the elderly have been conducted after single dose administration, for many drugs more clinically useful information will be obtained from studies carried out under continuous multiple dose conditions. Some pharmacokinetic age differences have been documented and tend to be consistent with age related changes in body composition, protein binding, hepatic drug metabolism, and renal excretion (Triggs and Nation, 1975; Crooks et al., 1976; Richey and Bender, 1977). However, apparent age differences in drug metabolism are probably multifactorial (Vestal et al, 1975).

2.1 Pharmacokinetics

2.1.1 Absorption - most drugs are taken orally and it is important that no change in the rate or amount of drugs absorbed from the gastrointestinal tract has been shown with ageing (Castleden, Volans and Razmond, 1977).

2.1.2 Distribution - after absorption, a drug rarely remains in the plasma alone, but is distributed to other parts of the body. There is insufficient evidence to date to draw any general conclusion on the effect of ageing on the apparent volume of distribution of drugs. In some it is unaffected, for example, nitrazepam, lorazepam, nordiazepam and propranolol, while for others it is increased, for example, diazepam, chloridazepoxide, and propicillin (Castleden and George, 1979 ; Simon et al., 1972; Wilkinson, 1978).

2.1.3 Elimination - since there is no reduction in drug absorption in ageing it is clinically important that the elderly are at risk from relative over-dosage of drugs due to inefficient pathways for drug elimination and metabolism. There are two major routes for eliminating drugs from the body - liver metabolism and renal excretion. Most drugs undergo metabolism prior to excretion via the kidney or in the bile. A few are not metabolised to any significant extent in the body and are excreted essentially unchanged in the urine. Changes in drug elimination rates with ageing are most important for those drugs with a narrow therapeutic index, such as digoxin, aminoglycosides and hypoglycaemic agents. Defective elimination means that the tissue concentration and therefore the pharmacological effect of most drugs is greater in the elderly for a given dose, and this is a major cause for the increased incidence of adverse drug reactions in elderly patients.

Renal elimination - It is not well established that glomerular filtration and tubular secretion of drugs are reduced with ageing even though there may be no clinical evidence of renal failure (Davies and Shock, 1950; Molholm-Hansen et al, 1970; Castleden, 1978). The blood urea and serum creatinine concentrations are often within normal range despite a creatinine clearance of less than 50 mls per minute. Although this is unimportant for drugs with wide therapeutic ratios such as penicillin, a clear correlation has been established between renal function, ageing and digoxin toxicity (Ewy, Kapadia et al, 1969; Smith and Haber 1970). It is also unwise to use the aminoglycosides in elderly patients unless facilities for estimation of plasma drug concentration exist.

Hepatic metabolism - Since hepatic function and hepatic blood flow fall with ageing, it is not surprising that the elderly eliminate many drugs which are metabolized in the liver more slowly than the young (Castleden and George, 1979). To date there is sufficient work on first pass extraction and hepatic blood flow to suggest that any drug with a high extraction ratio will be eliminated more slowly in the elderly, and thus, if they are given the same dose as the young, they will have high plasma concentrations for longer. No such definite general pattern exists for drugs with lower extraction ratios except that the rate of clearance is never quicker in the elderly (Triggs and Nation, 1975; Wilkinson 1978). With drugs of a low extraction ratio it is important that the induction of drug metabolism may be reduced in the elderly (Salem et al., 1980).

2.2 Pharmacodynamics

Evidence for alterations in pharmacodynamics with ageing is at a preliminary stage, but strongly indicates that drugs acting on the central nervous system produce an enhanced response for a given plasma concentration. In other systems, particularly the cardiovascular, it would seem that this response is decreased with ageing. A major problem in this field is that many studies have compared geriatric patients and young normal healthy subjects. Thus pharmacodynamic changes apparently due to ageing may be explained sometimes by concomitant disease in the elderly. For example, concomitant disease may upset compensatory mechanisms which normally minimise unwanted effects of a drug; an example of this is postural hypotension which is a particular hazard in the elderly when certain drugs are used. Baroreceptor activity has been shown to decrease with ageing, mainly due to atherosclerosis, but also to autonomic neuropathies (Gribbin et al, 1971). There is also a greater sodium loss from diuretics secondary to a decreased number of nephrons, and hence a decreased ability to conserve sodium ions (Swales, 1979). There may also be disease of the myocardium so that stroke volume and heart rate cannot be increased.

Although there is some evidence that end organ or receptor response is decreased with ageing (Vestal et al, 1979; Schocken et al, 1979; Dillon et al., 1980), additional research is necessary to study mechanisms at the molecular, cellular and physiological levels in both animals and man.

Thus, the elderly differ from the young in the quantity of drug presented to the target organ (pharmacokinetics), and possibly in the sensitivity of that organ to the drug (pharmacodynamics). In spite of this, drugs tend to be taken in similar doses by both age groups, and it is not surprising therefore that overdosage occurs more commonly in the elderly.

Although such knowledge has been present for a number of years there are very few drugs for which a specific geriatric dosage is recommended, and dosage regimens for new drugs are still established on data obtained in younger individuals. Since it is not yet possible to draw firm guidelines on all the effects of ageing on drug pharmacokinetics and dynamics, many more carefully designed studies are required involving normal healthy elderly volunteers.

3. SELF-CARE AND SELF-MEDICATION AND THE ELDERLY PATIENT

From several studies on self-medication it appears that about 80% of the examined elderly patients practiced self-medication once per year and about 40% practiced it in a 48 hour period. (Adamson & Smith, 1978; Calkhoven (1980)). It was also found that the use of medicines by the elderly increases with the age of the patient. This applies in particular to elderly women. And it was shown that there is a continuous need for education concerning non-prescription medications (Adamson and Smith, 1978).

Other studies have confirmed that elderly people have a high consumption of medicaments (Burger, 1979; Merkus, 1978). This consumption can lead to interaction with prescribed medication, to undesired side-effects and even to intoxications. Moreover, as noted above, one should take into account the fact that elderly people may suffer from an impaired renal function and a reduced detoxifying capacity of the liver.

The self-medication options for the elderly include many varieties of herbal medicines and drugs. The justification of self-medication lies in the self-limiting nature of many diseases. It should be appreciated that self-medication is only one aspect of self-care, the encouragement of which is of great importance in meeting the demands for health care in both developed and developing countries.

4. COMPLIANCE BY ELDERLY PATIENTS

"Compliance", a more common term than "discipline" or "cooperation", refers to the punctiliousness of patients in following physicians' orders. Although little studied before 1960, the subject attracts considerable interest today. Over 1000 papers and important meetings have been devoted to it (Graham et al., 1979; Hulka et al., 1976; Sackett, 1977; Stewart et al., 1972; Vestal, 1978; Wade, 1979). As noted by Nemitz et al, 1978, age appears to be a factor contributing to noncompliance by patients at both extremes in the lifespan: in children or adolescents inadequately supervised by their parents, and in the elderly after the age of 60.

Drug compliance is not the only form of compliance to be considered in geriatrics. It is also important to be able to assess cooperation by the elderly patient in matters such as: diet, in the case of diabetes or severe heart failure and physical treatment, in the case of stroke or rheumatic disorders. There is little known about the extent of compliance with other forms of treatment, such as occupational therapy, social support or psychological help.

Cooperation is normally judged inadequate (Andersen, 1974) if the patient consciously or unconsciously makes a qualitative or quantitative change in the prescribed treatment, thus jeopardizing its success. Non compliance may take the form of: failure to take drugs at certain times, interruption of treatment, errors in doses, drug-taking at incorrect intervals and addition of other drugs.

The proportion of patients of all ages regarded as noncompliant varies, according to different studies, from 25% to 59%. It is probably more useful to bear in mind that in 4-35% of these patients, errors influence the quality of treatment (Stewart et al, 1972). Advancing age in itself does not seem to be a significant factor affecting the quality of compliance (Graham et al 1979). Above all, compliance is affected by related factors such as: polypharmacy due to multiple pathology, memory impairments and visual impairment.

Moreover, at a given level of noncompliance, the older patients are generally at greater risk of therapeutic failure or adverse drug reactions than younger patients.

5. DRUG MISUSE IN THE ELDERLY

Misuse/abuse of prescription drugs by the elderly are not generally recognized unless the problem reaches emergency dimension and is brought to light in a medical ward or a psychiatric clinic. Nearly 20 per cent of the patients entering the geriatric service of a general hospital display symptoms attributable to the effects of prescription drugs (Wynne and Heller, 1973; Pascarelli, 1974).

6. STRATEGIES FOR RATIONAL DRUG THERAPY FOR THE ELDERLY

6.1 Is drug therapy required?

It is important to realize that many of the diseases or symptoms from which the elderly suffer are doing the patient no immediate harm and do not require treatment. Certainly, there is no need to prescribe a different drug for each disease or symptom simply because of the multiple pathology present in the elderly. Indeed, it is surprising how often the elderly are better off without some drugs. Many old people admitted to hospital or reviewed during long term hospitalization improve greatly when the regimen of drugs that they have been taking is stopped (Burr et al., 1977; Learoyd, 1972). This also means that a drug should

not be used for longer than necessary: the need for repeat prescriptions should be reviewed at periodic intervals. These edicts do not mean, however, that drugs should be withheld on account of old age, particularly when appropriate drug treatment can improve the elderly person's quality of life.

However, drug treatment should never be regarded as a substitute for time spent in helpful advice or by endeavouring to plan treatment by simple adjustment of the daily living of the elderly individual. Success in therapy depends often on the confidence of the patient in his doctor and on the bond of affection formed in the relationship. The use of drugs has to be combined with attention to the mental health and social circumstances of the old person.

6.2 If drug treatment is required, which treatment is appropriate?

The margin between therapeutic effect and toxicity is so small in many cases that a drug which is indicated for a particular condition in younger patients may be unsuitable in the elderly with the same condition. For example, in the treatment of gastric ulceration, carbenoxolone in older patients may result in hypocalcemia with its complications.

6.3 Is the patient being asked to take more drugs than he can tolerate or manage?

The fewest drugs that the patient needs should always be used. The more drugs prescribed the greater the chance of adverse drug reactions or drug interactions, thus the likelihood of toxicity increases as the number of drugs prescribed rises. In addition, there is an increased likelihood of errors by the patient in taking the medication leading to a possible lack of efficacy or an increase in toxicity. Medication errors, especially of omission, non-comprehension and non-compliance with medication instructions are common in the elderly (Schwartz et al, 1962; Parkin et al., 1976). Slowness of comprehension and lapses of memory, particularly short term memory which deteriorates with age, make it difficult for the elderly to manage complex drug regimens.

6.4 Which type of preparation to be used?

Apart from the total number of drugs prescribed, the dosage form, and the size, shape and colour of tablets and capsules and their similarity to one another, are all important considerations (Mazullo, 1972). Many older people have difficulty in swallowing, consequently large tablets and capsules should be avoided. There is a good case for the use of liquid preparations such as syrups for many patients, or of effervescent tablets. On occasion, the suppository may be the most suitable method of administration, for example, indomethacin at night for relief of nocturnal pain and morning stiffness of rheumatoid arthritis.

Many tablets and capsules of widely differing pharmacological actions are of similar size, shape and colour. This causes confusion for the patient: the loss of vision of the elderly in particular makes it difficult for them to determine which preparation they are taking. Touch and colour vision are however, well preserved in the elderly. Thus, preparations to be used together should not be of the same colour or the same shape. The more distinctive the pill is, the easier it is to use it.

6.5 Should the standard dosage or dosage schedule be modified?

As a rule, the elderly patient requires smaller doses of drugs than are customarily given to the young adult, e.g. the starting dose of thyroxine and the maintenance dose of digoxin. Drugs usually given in reduced dosage in the elderly are listed in Table 1. Whenever possible, intermittent schedules, such as drugs given on alternate days or 5 days a week, should be avoided, since they are rarely followed with accuracy. Once or twice daily dosage is the ideal, whenever feasible. Apart from convenience to the patient and thereby better patient compliance, once daily dosage at night, for example of psychotherapeutic drugs (Ayd, 1972, 1974) may well avoid troublesome adverse reactions since the patient would be asleep when these effects would be most troublesome. Other drugs may be best given as a single dose in the morning, for example diuretics.

6.6 Which side effects are likely to occur? Which drugs should be avoided if possible?

(See Table 2).

The elderly differ from the young in that drugs more frequently lead to confusion and vague ill health. Drugs which act on various systems such as the gastrointestinal tract for example, are more apt to produce gastrointestinal upset in the aged. Similarly, psychotherapeutic drugs may frequently induce markedly abnormal behavioural responses in older patients, while in younger patients these are much less common (Davison, 1971, 1972).

6.7 Should the drug be specially packed and labelled?

Where possible, drugs prescribed for the elderly living at home should be packaged in readily opened containers so that disabled patients in particular are able to use them (Law and Chambers, 1976). Clear labelling and listing indication in large print are also very important.

6.8 Can the patient living at home manage self-administration?

The elderly patient should be taught to understand his drugs, particularly their relative importance to his well being, and time should be spent to educate him in their use and administration (Gibson and O'Hare, 1968). Sometimes it may be necessary to provide clear instruction in writing about the manner in which a drug should be taken or to suggest the use of a diary or calendar to record daily drug administration (Wandless and Davie, 1977).

Collaboration with a responsible and interested relative, neighbour or friend can be helpful. Even with these and other considerations, discussed above, some drugs are best kept in the custody of others. Recent surveys have shown that many elderly patients living at home have potent drugs prescribed for them when they are mentally unfit to be responsible for their use (Shaw and Opit, 1976). It is imperative in such cases that a responsible relative should have charge of drug treatment. If there are no relatives it may be necessary to ask the community nurse to administer drug therapy. Sometimes these arrangements are necessary for physical reasons, for example, an elderly diabetic with impaired vision cannot be expected to measure out an injection of insulin with safety.

6.9 Is there a need for continued medication?

Because a drug such as digoxin has been prescribed in an acute episode, for example, atrial fibrillation complicating pneumonia, there is no reason for its continued use once the acute episode has been satisfactorily treated. The same is true of many drugs commonly prescribed. It is useful to review treatment regularly and discontinue drugs no longer wanted (Burr et al., 1977; Learoyd, 1972).

Elderly patients tend to hoard drugs (Law and Chambers, 1976). Accumulation of medication will only serve to confuse the patient and encourage use of drugs from prior treatment programme. To aid in the review of old, and current medication, patients should be encouraged to bring their containers to consultations in private practice and also in hospital outpatient departments.

Finally, it is worth re-stating that many of the drugs prescribed for elderly patients are prescribed, not for recognized syndromes but for symptoms related to the multiple diseases associated with the ageing process. In addition, the elderly have difficulties in adapting to their physical, psychological and social environments, which may be expressed as symptoms. It is important to recognize that the symptoms of elderly patients do not invariably require the use of drugs, and even when they are indicated, they must be used carefully. This applies particularly to the psychotherapeutic drugs (Hollister, 1975; Learoyd, 1972).

7. RECOMMENDATIONS

Recognizing that ageing is not a disease and that as such is not treatable by medicaments, the Technical Group on Use of Medicaments by the elderly makes the following recommendations, based on the preceding report:

1. That standardized methodology, such as Defined Daily Dose (DDD), be adapted for comparative studies, between countries and regions, of drug utilization in the elderly, and also for longitudinal assessment of the effects of educational programmes aimed at promoting rational drug therapy in the elderly.
2. That the activities of the Drug Utilization Research Group currently sponsored by the WHO Regional Office for Europe be extended to other regions. The group should also be invited to study comparisons of morbidity statistics in elderly populations from different countries.
3. That educational programmes in geriatric clinical pharmacology and therapeutics (including non-drug therapy) be developed in both the undergraduate and postgraduate curricula of all health professionals. In particular, the contribution of nursing staff and pharmacists would be enhanced by inclusion of geriatric clinical pharmacology in their curricula.
4. That the involvement of drug information pharmacists (a designation which is perhaps more suitable for those individuals known as clinical pharmacists in some countries) be encouraged in geriatric medicine as practiced in ambulatory, hospital and long term institutional care.
5. That geriatric patient education programmes be expanded to promote understanding of therapeutic objectives.
6. That therapeutic regimens for geriatric patients be regularly reviewed by all members of a health care team in the institutional setting or by the prescribing physician in the community.
7. That research be encouraged in geriatric clinical pharmacology involving both patients and healthy volunteers, with an emphasis on drug response as well as on drug distribution and elimination. In addition, particular attention should be accorded to drugs with special problems when used in elderly patients, e.g. those with a narrow therapeutic index such as cardiac glycosides.
8. That basic research be sponsored in human physiology and the pharmacology of ageing, with the new development and further evaluation of animal models (perhaps including primates).

9. That drug regulatory agencies should require the inclusion of relevant, geriatric patient groups in all phases of new drug evaluation which would allow the preparation of appropriate drug information for prescriber and patient.

10. That health education in the area of self-medication be developed as a component of general self-care programmes for the elderly and that health care professionals take responsibility for such programmes. Further research to elucidate the optimal role of self-care in the elderly population is needed.

11. That the established principles of geriatric pharmacotherapy outlined in this report be more widely utilized in patient management to promote optimal drug use and compliance in the elderly. Furthermore, additional research is needed to develop new methods of changing prescribing practice and improving compliance. WHO sponsorship in this area would be valuable.

12. That WHO should specifically address issues associated with the use of medicaments in the elderly when planning and implementing programmes directed to:

- collation and analysis of epidemiological data on drug usage and drug induced adverse reactions;
- transfer of information between drug regulatory agencies;
- sponsorship and coordination of drug research.

Table 1

Examples of drugs usually given in reduced dosage in the elderly

Drug	Possible consequences of standard dosage regimen
Aminoglycosides	Ototoxicity and retrotoxicity
Benzodiazepines	Unwanted CNS depression more common with larger doses
Carbamazepine	Drowsiness or ataxia may develop
Chlormethiazole	Confusion can occur with larger doses
Digoxin	Digitalis toxicity
Haloperidol	Danger of severe extrapyramidal signs
Levodopa	Hypotension common
Metoclopramide	Confusion common
Pethidine (meperidine)	Respiratory depression
Thioridazine	Confusion common
Thyroxine	Myocardial infarction
Vitamin D	Renal toxicity

Table 2

Drugs with potentially severe or unusual side effects in the elderly

Drug	Unwanted effect
*All barbiturates	Confusion
*Bethandine	Severe postural hypotension
Benzhexol (trihexphenidyl)	Visual and auditory hallucinations
*Carbenoxolone	Fluid retention and congestive cardiac failure
Cardiac glycosides	Behavioural disorders, abdominal pain, fatigue
*Chlorpropamide	Hypoglycemia
Chlorpromazine	Postural hypotension, hypothermia
*Chlorthalidone	Prolonged diuresis, incontinence
*Debrisoquine	Postural hypotension
Disopyramide	Urinary retention
Emepronium bromide	Mouth and esophageal ulceration, bromism
Ethacrynic acid	Deafness
*Guanethidine	Postural hypotension
Indomethacin	Aplastic anemia (lower incidence than phenylbutazone)
Isoniazid	Hepatotoxicity
Mefenamic acid	Diarrhoea
Methyldopa	Drowsiness and depression
*Nitrofurantoin	Peripheral nephropathy
Oestrogens	Fluid retention and congestive cardiac failure
*Pentazocine	Confusion, variable efficacy
*Phenylbutazone	Aplastic anemia
Tetracycline	Rising blood urea in the presence of impaired renal function

*Drugs to be avoided in the elderly if possible.

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REFERENCES

- Adamson, K.A., Smith, D.L. (1978) - Canadian Pharmaceutical Journal, 4, 80
- Anderson, W.F. Administration, labelling and general principles of drug prescription in the elderly. Gerontologia Clinica, 16: 4 (1974)
- Boethius, G. Prescription of drugs 1970-1975 in the county of Jämtland, Sweden. Stockholm-Östersund, 1977 (ISBN 91-7222-182-8)
- Borda, I., Jick H., Slone, D., et al. : Studies of Drug Usage in Five Boston Hospitals. JAMA, 202(6): 170-174, Nov. 1967
- Burger, A.K.C. (1979) - Pharmaceutisch Weekblad, 114, 581. Holland
- Burr, M.I., King, S., Davies, H.E.F. and Pathy, M.S. (1977), Age and Ageing, 6, 38
- Bush, P.J., Rabin, D.L. : Who's Using Nonprescribed Medicines? Med. Care, 14(12): 1014-1023, Dec. 1976
- Calkhoven, J.E. (1980) - Huisarts en Wetenschap, 23, 226. Holland
- Cape, R. : Ageing: Its complex management. Harper & Row; Hagerstown, Maryland, 1978
- Castleden, C.M., 1978. Prescribing for the elderly. Prescribers Journal, Vol. 18, 90-94
- Castleden, C.M., George, C.F., 1979. The effect of ageing on the hepatic clearance of propranolol. British Journal of Clinical Pharmacology, Vol. 7, 49-54
- Cooper, J.W., Jr., Bagwell, C.G.: Contribution of the Consultant Pharmacist to Rational Drug Usage in the Long-Term Care Facility. J. Am. Ger. Soc., 26(11): 513-520, Nov. 1978
- Crooks, J., O'Malley, K., Stevenson, I.H.: Pharmacokinetics in the elderly. Clin Pharmacokinetics, 1: 280-296, 1976
- Davies, D.F. and Schock, N.W., 1950, Age changes in glomerular filtration rate, effective renal plasma flow, tubular excretory capacity in adult males. Journal of Clinical Investigation, Vol. 29, 496-507
- Dillon, N., Chung, S., Kelly, J. and O'Malley, K. 1980. Clinical Pharmacology and Therapeutics, Vol.27, 769-772
- Freeman, G.K. : Drug prescribing patterns in the elderly - A general practice study. pp. 223-228. In Drugs and the Elderly. Perspectives in Geriatric Clinical Pharmacology. Crooks, J., Stevenson, I.H. (Eds). University Park Press; Baltimore, Maryland, 1979
- Gibson, R.M., Mueller, M.S. and Fisher, C.R.: Age differences in health care spending. Fiscal year 1976. Social Security Bulletin 40 : 3-14 (1977)
- Graham, J.M. & Suppre, D.A.: Improving drug compliance in general practice. J. roy. Coll. gen. Pract., 204: 399 (1979)
- Gribbon, B., Pickering, T.G., Sleight, P. and Peto, R.: Effect of age and high blood pressure on baroreflex sensitivity in man. Circulation Research 29: 424-431 (1971)
- Guttman, D.: Patterns of legal drug abuse by older Americans. Addictive Diseases: An International Journal 3(3): 337-356, 1978
- Hollister, L.E. (1975) Journal of the American Medical Association, 234, 195
- Howard, J.B., Strong, K.E. Sr., Strong, K.E. Jr. : Medication Procedures in a Nursing Home: Abuse of PRN Orders. J.Am. Ger. Soc., 25(2): 83-84, 1977
- Howard, J.B., Strong, K.E. Sr., Strong, K.E. Jr. : Nursing Home Medication Costs. J.Am. Ger. Soc., 26(5): 228-230, May 1978

- Hulka, B., et al. Communication, compliance and concordance between physicians and patients with prescribed medications. Amer. J. Pub. Health, 66: 847 (1976)
- Ingman, S.R., Lawson, I.R., et al. : A survey of the prescribing and administration of drugs in a long-term care institution for the elderly. J.Am. Ger. Soc., 23(7): 309-316, July 1975
- Kalchthaler, T., Coccaro, E., Lichtiger, S.: Incidence of polypharmacy in long-term facility. J.Am. Ger. Soc., 25(7): 308-313, July 1977
- Kohn, R. & White, K.L. Health care: an international study. London, Oxford University Press, 1976
- Law, R., Chambers, C. (1976) - British Medical Journal, 1, 565
- Lawson, D.H., Jick, H.: Drug prescribing in hospitals: An international comparison. Am. J. Public Health 66(7): 644-648, July 1976
- Learoyd, B.M. (1972), Medical Journal of Australia, 1, 1131
- Mazullo, J.M. (1972) Clinical Pharmacology and Therapeutics, 13, 157
- Merkus, F.W.H.M. (1978) - Het voorschrijven van geneesmiddelen, Utrecht, Bohn, Scheltema & Holkema. Holland, p. 186-208
- Molholm-Hansen, J., Kampmann, J. and Laursen, H. 1970. Renal excretion of drugs in the elderly, Lancet, Vol i, 1170
- National Academy of Sciences: Study of health care for American veterans. Report to the Senate Committee on Veterans' Affairs. p. 15-16 (US Government Printing Office, Washington, 1977)
- Nemitz, I. & Schellin, J.L. Un aspect particulier de la pharmacothérapie: la compliance. Rev. med. Suisse Romande, 99: 451 (1979)
- Nordic Council, Statistical Reports of the Nordic Countries, nos. 35 and 36, 1979
- O'Malley, K., Judge, T.G. and Crooks, J. Geriatric clinical pharmacology and therapeutics: in Avery (Ed) Drug Treatment, p. 123-142 (Adis Press, Sydney; Churchill Livingstone, Edinburgh; Lea and Febiger, Philadelphia 1976)
- Parkin, D.M., Henney, C.R., Quirk, J. and Crooks, J. (1976) British Medical Journal, 2, 686
- Purola, T., Kalimo, E. & Nyman, K. Health services use and health status under national sickness insurance. Social Insurance Institution of Finland, 1974 (A:11/1974)
- Richey, D.P. and Bender, D.: Pharmacokinetic consequences of aging. Annual Review of Pharmacology and Toxicology 17 : 49-65 (1977)
- Sackett, D., ed. Workshop-Symposium on Compliance. Hamilton, McMaster University Medical Centre, 1977
- Schocken, D. and Roth, G.: Reduced beta-adrenergic receptor concentrations in aging man. Nature 267: 856-858 (1977)
- Schwartz, D., Wang, M., Feitz, L. and Goss, M.E.W. (1962) American Journal of Public Health, 52, 2018
- Shaw, S.M. and Opin, L.J. (1976) British Medical Journal, 1, 505
- Simon, C., Malerczyk, B., Muller, U. & Muller, G. 1972. Zur pharmakokinetik von propicillin bei geriatrischen patienten im vergleich zu jungeren erwachsenen. Deutsche Medizinische Wochenschrift Vol. 97, 1999-2003.

Smith, T.W. and Haber, E, 1970, Digoxin intoxication: relationship of clinical presentation to serum digoxin concentration. Journal of Clinical Investigation, Vol. 49, 2377-2386

Stewart, R.B. & Cluff, L.E. A review of medication errors and compliance in ambulant patients. Clinical pharmacology and therapeutics, 13: 463 (1972)

Swales, J.D. 1979, Pathophysiology of blood pressure in the elderly. Age and ageing, Vol. 8, 104-109

Triggs, E.J., Nation, R.L.: Pharmacokinetics in the Aged: A Review. J. Pharmacokinetics and Biopharmaceutics, 3(6): 387-418, 1975

Vestal, R.E., Norris, A.H., Tobin, J.D., Cohen, B.H., Shock, N.W., and Andres, R. 1975, Antipyrin metabolism in man: Influence of age, alcohol, caffeine and smoking. Clinical Pharmacology and Therapeutics, Vol 18, 425-432

Vestal, R.E. Drug use in the elderly: a review of problems and special considerations. A.D.I.S. Press, 1978

Vestal, R.E., Wood, J.J., and Shand, D.G., 1979. Reduced Beta-adrenoreceptor sensitivity in the elderly. Clinical Pharmacology and therapeutics, Vol. 26, 181-186

Wade, O.L. Compliance problems. Drugs and the elderly. London, Macmillan, 1979

Wandless, I. and Davie, J.W. (1977) British Medical Journal, 1, 359

Wilkinson, G.R. 1978. Effects of liver disease and ageing on the disposition of diazepam, chlordiazepoxide, oxazepam and lorazepam in man. Acta Psychiatrica Scand. Vol S274, 56-74

World Health Organization, Regional Office for Europe, Technical Advisory Committee on Health Care of the Elderly. ICP/ADR 018, Copenhagen, 1978

World Health Organization, Regional Office for Europe, Studies in Drug Utilization, European Series No. 8, Copenhagen 1979

World Health Organization, Regional Office for Europe, Ninth Symposium on Clinical Pharmacological Education in Drug Control, Copenhagen 1981 (in preparation)