Drug Treatment of the Elderly Patient

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Second edition

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Pitman

Preface
to the Second Edition

The second edition of a book requires perhaps even more justification than the first. This revision has become necessary because in the past few years there has been a substantial growth of interest in and knowledge of the problems of drug treatment in the elderly, reflecting increasing recognition of the importance of the subject. There has been much valuable work on drug kinetics, though it remains as yet unclear what general principles can be extracted from a mass of somewhat conflicting data, while the practical value of the information is unfortunately somewhat less than what might have been foreseen. A beginning has been made in the study of the very important topic of drug dynamics in relation to age and disease. New drugs have become available, or have been used in clinical practice in middle age for long enough for their values and potential dangers in the elderly to be recognised, and for reasonable suggestions for dose regimes in old age to become practicable.

The present edition remains personal in that we have continued to record our own experience and our own personal views, and these also have changed, at least in some areas, in recent years. Highly specialised topics such as cancer chemotherapy and drug treatment in ophthalmology and otology have again been omitted.

We are grateful to our colleagues for helping us to form the views expressed. They are largely responsible for anything that is right, and totally without responsibility for any errors, which remain our own. We are also particularly grateful to Pitman Books, and especially to Stephen Neal, for continued interest and stimulation.

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Preface
to the First Edition

The 12 per cent of our population that is over the age of 65 accounts for 33 per cent of the expenditure of the National Health Service, and an equivalent proportion of the drug bill. Approximately one in six of *all* old people, not simply those in hospital, takes three or more drugs a day, and perhaps one in sixteen, five or more a day. The incidence of drug reactions and interactions rises with the number of drugs taken, and an adverse drug reaction or an interaction between drugs is a common reason for admission of elderly people to hospital. These facts indicate the great practical importance of drug therapy in the elderly, yet there is very little useful guidance for those who prescribe drugs for old people. The subject attracts little attention in textbooks of medicine or pharmacology, though it is clear from everyday experience in geriatric medicine that the differences between the elderly, especially those over the age of 75 years, and the young and middle-aged in their responses to drug therapy are an important cause of morbidity and occasionally, indeed, of mortality in old age.

The purpose of the present book is to remedy this deficiency as far as is currently possible. We have attempted to deal both with important clinical problems requiring drug therapy in the elderly, and with important groups of drugs used in the treatment of disease in old age. Because of the lack of detailed factual information in the literature, we have necessarily recorded the results of our own experience and our own personal views. We have omitted some topics such as cancer chemotherapy, where specialised opinion is likely to be necessary before drug therapy is embarked upon, and certain other common topics, particularly in ophthalmology and otology, where again the prescriber would be best advised to seek specialist advice if he encounters problems outside those commonly met with at any age. We have attempted to tabulate the drugs commonly used in each clinical situation, and have given them their British and American proper names, together with the commonest of their trade names. Differences in official nomenclature on either side

of the Atlantic are a minor cause of difficulty, whereas the number and variety of trade names constitute a major problem in clinical practice.

We are grateful to our teachers and colleagues for many of the views expressed, and in particular to Dr. H. M. MacLeod for his detailed criticism of the manuscript, which has removed many errors from the text. Those that remain are our own, and any virtues are those of others.

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Part One **Principles**

Introduction

Prescribing for the elderly must be based on sound clinical principles, to ensure that they are not denied adequate therapy when this is indicated, nor needlessly exposed to potentially toxic drugs. There are eight questions which should always be answered before a drug is prescribed for the elderly.

Is drug therapy required at all?

For example, is a night sedative required to produce sleep, or would the patient settle with an empty bladder and rectum, or a warm room and a comfortable bed, or a hot milky drink? Would a night sedative be required at all if the patient abstained from drinking coffee late in the evening, or from taking large volumes of fluid just before retiring? Would an antidepressant drug be required if voluntary visiting were arranged, and the patient were no longer so lonely? Is a phenothiazine the best treatment for dizziness due to postural hypotension resulting from a hypotensive drug?

Is the choice of drug correct?

Diagnosis may prove difficult in many elderly people. Thus it is not difficult to confuse the facial appearance of Parkinsonism with that of depression or of hypothyroidism. A diagnostic error between these three conditions can clearly lead to serious misuse of drugs. Again, if cardiac failure is diagnosed when only dependent oedema is present, incorrect prescription of diuretics and digoxin can result. Confusion in the elderly is another common pitfall in diagnosis: it can be a manifestation of many different disease processes and frequently leads to inappropriate treatment. The slow, insidious, and cryptic presentation of many diseases can also give rise to serious difficulties in diagnosis, and so in rational prescribing. Further, the fact that

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most elderly people who are properly examined can be shown to have more than one disease process simultaneously is a standing temptation to the prescription of more than one drug. At all costs, a drug regime for an individual patient must be kept as simple as possible.

Is the dosage correct?

Almost without exception, the elderly require smaller doses of drugs than do people in earlier life. If the regular dose is prescribed, cumulation may result in toxicity. The position is not made easier by the fact that many drugs are, and continue to be, marketed in strengths too large for most elderly people, their principal consumers. Thus nitrazepam 2·5 mg is sufficient at night for many elderly people, though it is marketed in 5 mg and 10 mg tablets and the manufacturer's literature suggests that the standard dose is 5 to 10 mg. A few days of this dose, especially in elderly people of small build, may lead to drowsiness by day as well as by night.

What are the undesirable effects?

In addition to the common side effects of many drugs, such as nausea, vomiting, and skin rashes, the elderly react to many drugs by developing confusion, postural hypotension, and hypothermia. Unwanted effects also occur as a result of drug interaction and the risk of their occurrence increases with the number of drugs prescribed.

It is a good rule that if any elderly patient receiving a drug develops fresh symptoms, the possibility of these being due to the drug should be seriously considered, and, if possible, the drug should be withdrawn. There are few exceptions to this rule (see p6).

Is the choice of preparation correct?

Many older people have difficulty in swallowing, and some frequently prescribed drugs are large in physical size. Failure to take a drug is thus sometimes due to this simple physical difficulty. It is often worthwhile considering the use of liquid preparations, either in the form of effervescent tablets (e.g. potassium chloride effervescent tablets, B.N.F.) or as suspensions, liquids, or elixirs. Slow-release preparations can give rise to difficulty in the elderly, since intestinal

hurry can lead to failure of utilisation consequent on rapid passage of the drug through the gastrointestinal tract, and conversely, slowing of bowel transit times may lead to increased absorption resulting from increased time in contact with the gastrointestinal mucosa.

How can compliance best be ensured?

The most important single point in improving compliance is to ensure that drug prescribing is kept to the minimum, and that regimes are as simple as can be achieved. In hospital patients drug therapy should be regularly reviewed, and the simplest possible regime adopted. This is essential just prior to the patient's discharge home. Combined preparations may have a place at this point, as they often permit simplification. In some cases modification to allow once-weekly medication may be beneficial. For example, vitamin D for treatment of osteomalacia can be administered in one larger dose weekly, instead of a small daily dose. Under some circumstances the long-acting injectable phenothiazine fluphenazine decanoate (Modecate) can be given once a fortnight in place of thioridazine or chlorproma-zine three times daily.

Many old people are unable to deal with drugs presented in unusual ways, however appropriate these may be for younger people. Thus the bubble-pack presentation may be completely unusable and a package which is child-proof is likely to be granny-proof as well. Drugs for the elderly should be presented in wide-mouthed jars of clear glass, with simple screw or bayonet tops. Labelling should be appropriate to the vision of the patient, and the proper name for the drug should always be included on the label.

Also very important is deliberate teaching of the patient to take the drugs accurately. This may conveniently be done in the few days before the patient's discharge from hospital, when the drug regime on which the patient will be discharged has been finalised in the simplest possible form. A variety of aids to teaching may be used. The most satisfactory are the simplest, such as cards on which the names of the drugs are clearly written, together with the times of day at which they should be taken. The purpose for which each drug is being given, and perhaps an individual tablet, should be displayed as well. More complicated drug calendars, on which the patient ticks off each dose as it is taken, are perhaps more theoretically desirable, but are too complex for universal use. What is important is that the patient should be deliberately taught what to do, and should be

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supervised doing it, by nursing staff or the ward pharmacist, so that the effectiveness of the teaching can be monitored. There is no reason why a similar approach should not be adopted for elderly patients under treatment at home by general practitioners. The time required is not large, and is certainly well spent.

In many cases, however, patients will be unable to manage their own drug therapy, for a wide variety of reasons. It is useless to expect a blind, elderly diabetic to measure her own dose of insulin, or a confused patient, or one with failing vision, to look after even the simplest drug regime with any real accuracy. In these circumstances, actual administration of the drug must be placed in the hands of a responsible person: a member of the family, a neighbour, a home help, or a district nurse. The relatives or neighbours may well require as clear instruction in what to do as patients considered capable of managing their own drug treatment.

When can the drug be stopped?

There is a well-known tendency for drugs, once prescribed, to be continued for life. Often this is not necessary. Steroids, drugs for the treatment of Parkinsonism and for suppression of epilepsy should not be suddenly withdrawn. With these exceptions, it is usually safe to withdraw drug therapy from the elderly patient under careful observation and, in many cases, there is no need to restart drugs previously prescribed. There is no doubt that the indications for discontinuation of drug therapy should figure as large as those for its initiation.

Drug kinetics and dynamics

Rational drug therapy in the elderly requires a knowledge of the alterations in the kinetics and dynamics of drugs to be expected in old age, and of the common diseases requiring drug treatment. There is at present little information about drug dynamics in the elderly (i.e. the effects of drug concentrations upon receptor sites and mechanisms), but considerable knowledge of kinetics (i.e. the effects of metabolic and other body processes on drug concentrations), though the present situation is somewhat confused, and there are as yet few clearly established principles. A further important consideration is that of interactions between drugs, if only because multiple pathology in old age is a standing temptation to polypharmacy.

Drug kinetics may be considered under the headings of absorption, bioavailability, distribution, transport and protein-binding, metabolic degradation, and excretion. Drug interactions may operate at almost all these points.

Absorption of both water- and fat-soluble substances from the stomach and small bowel seems to be effectively as rapid and complete in the elderly as in the young, and there is no reason to suppose drugs to be preferentially affected. The small number of useful studies of the gastrointestinal handling of drugs suggest that there are few or no differences in the elderly. The bioavailability of a drug is defined as the proportional absorption into the systemic circulation of an oral dose compared to that of a parenteral dose. Since the liver removes from the portal blood flow a substantial proportion of many substances presenting to it (the first-pass effect), it might be expected that drugs which are extensively degraded in the liver might show a change in bioavailability with age. Though relatively few drugs have been studied in the elderly both after oral and intravenous administration, as is necessary for the accurate measurement of bioavailability, it is clear that some drugs, extensively metabolised in the liver to pharmacologically inert metabolites (e.g. propranolol), show a substantial increase in their bioavailability in the elderly. This is probably the product of reduced hepatic blood

flow and drug metabolism. It must be emphasised that there are as yet no clear examples of a reduction in bioavailability with age.

Important drug interactions may result from alterations in gastrointestinal motility and from the formation of insoluble and therefore non-absorbable complexes within the lumen of the bowel. Drugs with an anticholinergic action, such as propantheline, the tricyclic antidepressants, and the phenothiazines, may all reduce the rate of transit, and therefore, by allowing more time for absorption to occur, increase the magnitude of absorption. Drugs which increase motility, such as laxatives, may prevent adequate absorption, particularly of slow-release preparations. Insoluble metal complexes are formed between tetracycline and calcium and iron salts, and the absorption of tetracycline may be greatly reduced if preparations of calcium or iron are being given concurrently. The absorption of iron may also be reduced.

The transport of drugs in the plasma largely occurs by variable degrees of attachment to serum albumin and other serum proteins. The crucial factor in the therapeutic activity of a drug is its free or unbound concentration. In healthy old people, serum albumin concentrations are very little lower than in younger people, but substantial reductions are commonly encountered in sick old people. It appears that for the small number of drugs for which this has been studied, protein-binding is reduced with age, and this reduction is associated both with the minor age-related reduction in serum albumin, and the larger disease-related reduction. In clinical practice, the protein-binding of drugs cannot be easily evaluated, and it remains doubtful whether these changes are of clinical importance.

One of the principal mechanisms of drug interaction is displacement of one drug by another from protein-binding sites, with an increase in the concentration of free drug. Thus salicylates and phenylbutazone may displace tolbutamide, and so result in an unexpected increase in the latter's hypoglycaemic effect. These and other drugs may displace warfarin, and so cause an increase in anticoagulant effect. These displacement effects may perhaps be greater in the elderly than in the young, but are likely to be relatively brief and transient, since metabolic degradation and excretion mechanisms operate upon free drug concentrations, and a new equilibrium is rapidly established.

Little is known about the distribution of drugs in the body in the elderly. The reduction in lean body mass that occurs in old age could reduce drug distribution volumes, and this may be a partial explanation for the higher serum concentrations of some drugs (e.g. digoxin)

found in old people on a constant dose. Since body fat increases with age, it might be expected that volumes of distribution of predominantly fat-soluble drugs would increase with age. This may be so, but it has yet to be shown that the change in steady-state concentrations of drugs of this kind is clinically important.

The liver is the principal site of metabolic degradation of drugs, which occurs by a variety of biochemical mechanisms. Although there is evidence of minor degrees of decline with age in hepatic metabolic activity, there is as yet little indication that this is of much importance in relation to drug degradation, except in respect of changes in the first-pass effect, as described above. A further difficulty results from the formation by the liver of pharmacologically active metabolites. If this is delayed and prolonged, the effective drug action will also be prolonged. This has been demonstrated reasonably conclusively for some drugs, such as diazepam.

Most metabolic alterations of drugs in the liver result in their inactivation, and conversion into a more soluble form which can then be excreted in the urine or bile. These metabolic alterations occur principally in the microsomes, and the activity of the microsomal enzymes has been shown to be greatly affected by a variety of substances, including in particular several commonly used drugs. These mostly induce greater enzyme activity, and therefore increase the rate of metabolic degradation of other drugs. When they are stopped, there may be a rebound effect, of decrease in degradation rate. Thus phenobarbitone may increase the rate of metabolism of drugs such as tricyclic antidepressants and phenytoin, with a consequent decrease in their action. This enzyme induction may be less effective in old age, with a consequent reduction in the magnitude of drug interactions of this type. On the other hand, two drugs may compete for the same hepatic metabolic mechanisms, so that the rate of metabolism of each drug is decreased and the effects of both increased.

The excretion of drugs may be by the biliary route, or in the urine, as a result either of glomerular filtration or renal tubular secretion or both. The combination of age- and disease-induced reduction in hepatic blood flow, due for instance to cardiac failure, may reduce the biliary excretion of drugs such as digoxin and effects of this kind may be important in other connections. There is, however, excellent evidence that the effects of age on renal function constitute a most important mechanism for alteration of drug elimination in the elderly. Over the age of 40, both the glomerular filtration rate and renal tubular secretion decline by approximately 1 per cent per year,