DRUG Consultant

The Pocket Clinical Guide
to Drugs and their Usefulness

1985-86

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to Drugs and their Usefulness

Based on the British National Formulary

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The drug information and dosages in this book are based on research and consultations with authorities in medicine and pharmacy. A conscientious effort has been made to ensure that all the information contained in this book is accurate and in accord with accepted standards at the time of publication. However, the *Drug Consultant* is intended to be a pocket book for rapid reference and it should be supplemented as necessary by the medical literature and the FDA-approved package insert.

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IN MEMORIAM

George Ronald Brown
1920–1984

Arrangement of Information

Arrangement of the text
The main text consists of classified notes on drugs and preparations used in the treatment of diseases and conditions. These notes are split into 15 chapters, each of which is related to a particular system of the human body or to another main subject (infections, vaccines etc.). Each chapter is divided into sections which begin with appropriate *notes for prescribers*. These notes are intended to provide information to doctors, pharmacists, nurses, etc. to facilitate the selection, dispensing, and administration of suitable treatment. The notes are followed by details of relevant drugs and preparations.

Guidance on prescribing
This chapter includes information on prescription writing, prescribing for children and elderly patients, and prescribing for patients with liver or kidney disease and in pregnancy or lactation. Information is also given on adverse reactions, controlled drugs, and drug dependence.

Emergency treatment of poisoning
The main intention of this chapter is to provide information on the management of acute poisoning when first seen in the home, although certain aspects of hospital-based treatment are briefly mentioned.

Drugs
Drugs appear under their official names (United States Pharmacopeia, USP), or their nonproprietory United States Adopted Name (USAN). If there is a drug of choice, information on it is usually given first; otherwise the drugs are arranged alphabetically.

Preparations
These usually follow immediately after the drug which is their main ingredient. They are printed in text-sized type. Preparations are included under a nonproprietary name only if (a) they are marketed under such a name, (b) various proprietary products are available that comply with the nonproprietary description, or (c) they may be prepared extemporaneously. If proprietary preparations are of a distinctive color or flavor this is stated.

Compound preparations
The indications, cautions, contraindications, side effects, and drug interactions of all constituents should be taken into account in prescribing; usually the ingredients should be looked up separately, or other sources consulted.

Prices
The relative price bands (see inside cover) have been calculated from the Drug Topics Redbook 1984. These prices are based on the average wholesale price to the pharmacist. Relative price bands are omitted from statements on investigational drugs. A price average is used for generic drugs.

Preface

The Drug Consultant is a pocket book for those concerned with the prescribing, dispensing and administration of medicines.

Information is included on the products available to prescribers in the United States and some investigational drugs that are expected to be available. The entries, coupled with the relevant notes for prescribers, are intended to help in the choice of appropriate treatment of each patient.

Most of the preparations follow immediately after the notes for prescribers with which they are associated. It is considerd that this arrangement will help in the selection process.

Good prescribing requires careful consideration of the needs of the patient and the condition being treated; these factors may result in a limitation of choice. However, where there is a choice of a number of suitable preparations to treat a particular disease or condition the price bands may be used in making a selection on a basis of cost.

It should be emphasized that cost-effective prescribing must take into account other factors such as dose, frequency and duration of treatment that affect the total cost. The use of more expensive drugs is also justified if it will result in better treatment of the patient or a reduction of the length of an illness or the time spent in a hospital.

The Drug Consultant is intended to be a pocket book for rapid reference and so cannot contain all the information necessary for prescribing and dispensing. The information should be supplemented as necessary from specialized publications. Manufacturers' directions or FDA-approved labeling (package insert) are available for most proprietary medicines and these should also be consulted. Less detail is given in the chapters on malignant disease and immunosuppression, and anesthesia, as it is expected that those undertaking treatment will have special training in these areas.

Acknowledgements

The Drug Consultant is based on the British National Formulary (B.N.F.) which is published under the guidance of the Joint Formulary Committee of the British Medical Association and The Pharmaceutical Society of Great Britain. G. R. Brown was the Executive Editor of the first and subsequent editions of the B.N.F. published in the format on which this book is based. G. R. Brown is listed as an editor of the Drug Consultant out of respect for that contribution. The responsibility for the U.S. edition of the B.N.F. — the Drug Consultant — resides with the U.S. publisher, M.J. Powers and Co. Publishers, Inc.

Many people have played important roles in bringing this book to completion. In the United Kingdom, the Joint Formulary Committee under the Chairmanship of Professor Owen L. Wade gave its blessing to the project, and enthusiastic support for the completion of this U.S. edition has been given by Bernard Yates of the Pharmaceutical Press, Publisher of the B.N.F., and Ainley Wade and Frank O. Wells, Secretaries to the Joint Formulary Committee.

Mike Gerow, of Reproduction Typographers, provided technical support for the conversion of the British computer tape to a format for U.S. text editing. William Bailey of Basis, Inc., provided the computer program to convert the B.N.F. index to a database of all United States pharmaceuticals. William Vallario, RPh, of Rogers Pharmacy, cheerfully helped the editors find information on drug dosage forms and prices not included in standard references.

In addition to paying tribute to the advisors and supporters, two staff editors should be recognized for their extraordinary contributions to the Drug Consultant. Marie Luciani, Chief Copy Editor and Linda Smith, Production Editor, both supervised all the changes in this book.

Contents

Guidance on Prescribing

General Information

Medicines should be prescribed only when they are essential, and in all cases the benefit of administering the medicine should be considered in relation to the risk involved. This is particularly important with pregnant patients where the risk to both patient and fetus must be considered, as there are many drugs for which there is not sufficient evidence to ensure that they are entirely harmless to the fetus, especially during the first trimester of pregnancy.

NAMES AND ABBREVIATIONS. In general, names of drugs and directions for use should be written *in full*. Abbreviations, even those in common use, should be avoided as they may be misinterpreted. The abbreviation "O.D." may mean either "every day" or "right eye", and mistakes may occur. Similarly, when a drug name includes a number, such as 5-FU or 6-thioguanine, it is best to omit the number. In some cases, nurses and pharmacists have mistaken the number for the dose, and administered 5 tablets of fluorouracil or 6 tablets of thioguanine.

NON-PROPRIETARY NAMES. It is recommended that where non-proprietary (generic) names are given, they should be used in prescribing. This will normally enable any suitable product to be dispensed, thereby saving delay to the patient and frequently additional expense. Since many states have complex laws requiring generic dispensing of drugs, a prescription written generically is more likely to comply with regulations. Too often, a prescription written by brand name will not comply with state law and will not be valid for dispensing. The only exceptions are in those few instances (such as lithium carbonate tablets) where potential bioavailability problems can compromise the well-being of the patient. In these cases, the brand name should be used in prescribing or the manufacturer's name stated on the prescription.

PROPRIETARY NAMES. The names followed by the symbol® are or have been used as proprietary names in the United States. These names may in general be applied only to products supplied by the owners of the trademarks.

DOSES. The doses stated in the *Drug Consultant* are intended for general guidance and represent, unless otherwise stated, the usual range of doses that are generally regarded as being suitable for adults. Unless otherwise indicated the quantities are those generally suitable for administration as a single dose in part of a divided dosing schedule.

DILUTION. Where practical, orders should be written for commercial dosage forms, and smaller doses should be prepared by measuring out smaller portions of the original dose. Dilution may sometimes be accomplished by the patient, the pharmacist, or a parent or nurse responsible for the patient's care. Liquids are generally diluted with water or a vehicle similar to that used in the original formulation, tablets or capsules are made into powders and diluted with lactose, and ointments or creams are diluted with a suitable commercial vehicle. While this type of dilution may facilitate administration of small doses, it may also reduce the chemical, physical and bacteriologic stability of the preparation. On occasion, a solution may precipitate and turn into a suspension. Because of these risks, orders for diluted medications should be written for the smallest practical quantities.

STRENGTHS AND QUANTITIES. The strength or quantity to be dispensed should always be written out by the presciber. This applies even in those cases where the drug is supplied in only one strength, since this practice may help avoid errors in dispensing and avoid delays in reimbursement when the order is covered by a prescription plan. Providing the strength of the drug may help avoid confusion between two drugs with similar names. Similarly, some reimbursement plans may refuse to pay for prescriptions which are not filled out completely on the plan form. Since these decisions are usually made by clerical personnel with little opportunity to exercise discretion in these matters, the patient may be deprived of reimbursement because of an otherwise trivial omission.

CONTROLLED DRUGS. A prescription for a controlled drug is subject to a wide variety of Federal and State regulations. Familiarize yourself fully with the rules of your state, since state laws vary widely and are generally more restrictive than Federal regulations. The state laws and regulations will usually apply to the quantity which may be dispensed at one time, the number of times and the interval at which the prescription may be refilled, and the information which must appear on the prescription form. While the advice given in this section is often overlooked in general prescribing practice, it is essential that it be followed when prescribing controlled substances. In some states, the patient's address must appear on the prescription form and the name must be provided by the prescriber. The pharmacist may not obtain this information from the patient at the time of dispensing.

HEALTH AND SAFETY. The *Drug Consultant* is intended for the guidance of medical practitioners, pharmacists, dentists, nurses, and other workers who have the necessary training and experience to interpret the information it provides. It is intended as a reference book for the pocket, and should be supplemented by a study of more detailed publications when required.

Note that neither the information provided herein, nor the official package insert, restricts the practitioner in use of commercially distributed medications. The Food and Drug Administration has noted that often new uses for established drugs are reported in the professional literature before these

uses can be incorporated into the package insert. The prescriber should, however, be fully familiar with the literature before using a drug in a manner not consistent with the FDA approved literature, since nurses and pharmacists are entitled to request documentation before administering or dispensing drugs in doses or for uses which are not listed in the package insert.

When handling chemical or biological materials particular attention should be given to the possibility of allergy, fire, explosion, radiation, or poisoning. Some substances, including corticosteroids, antibiotics, phenothiazine derivatives, and many cytotoxic compounds, are irritant or very potent and should be handled with caution. Contact with the skin and inhalation of dust should be avoided. Consider the use of special safety equipment, such as gloves and vertical laminar flow hoods, when dealing with chemotherapeutic agents.

LABELLING OF CONTAINERS WITH THE NAME OF THE PREPARATION. It is generally recommended that prescription containers be labeled with the name and strength of the drug dispensed. This information facilitates taking a patient medication history, avoiding potentially harmful drug interactions, and could speed up treatment in the case of accidental poisoning. Many states have made labeling of prescription containers a requirement, but these regulations are not always wisely written, and prescribers should familiarize themselves with the applicable regulations wherever they practice.

In some states, pharmacists are required to label the prescription container with the brand name of the product they dispense, even if the prescription is being filled in a generic manner. When the prescription is filled generically, but labeled with the brand name of a small manufacturer, the benefits of labeling may be lost. Neither patient nor physician may be familiar with the brand name, and identification of the drug may be delayed if the manufacturer is not listed in the commonly used reference sources. For prescribers practicing in areas with this type of regulation, it is usually advisable to write "label generic name" on the presciption, as this will assure uniform identification of the product, regardless of the manufacturer.

Prescription Writing

The goals of effective prescription writing are as follows:

1. To convey an order for medication to be dispensed to the patient;
2. to communicate with sufficient clarity so that the risk of error in dispensing or administration of medication is minimized;
3. to communicate in such a manner that errors in prescribing may be detected and corrected before the drug can be administered to the patient; and
4. to comply with any rules governing prescribing which could affect the patient's ability to obtain either the drug or reimbursement for the cost of the medication.

To accomplish these goals, the following recommendations are made:

(a) For solids, quantities of 1 gram or more should be written as 1 g etc. Quantities less than 1 gram should be written in milligrams, for example 500 mg, not 0.5 g. Similar quantities less than 1 mg should be written in micrograms, not 0.1 mg. Micrograms should **never** be abbreviated.

(b) When decimals are unavoidable a zero should be written in front of the decimal point where there is no other figure, for example 0.5 ml, not .5 ml.

(c) When it is necessary to use measures in the apothecary system, do not use abbreviations in order to prevent confusion between "grains" and "grams."

(d) As a general rule, avoid abbreviations. Misinterpretation of abbreviations is a common source of error. Oral drops have been instilled into the eye because the abbreviation "O.D." meant to mean "every day" was taken to be "right eye". Similarly, overdoses have occurred when "QD", also used for "every day" was interpreted as "QID".

(e) The volume of measurement should be milliliter, not cubic centimeter.

(f) Dose and dose frequency should be stated. For liquid medicines, doses should preferably be stated in terms of 5-ml and 10-ml units. Because of variations in the volume delivered by household teaspoons, patients should be provided with, or encouraged to obtain standard medicinal teaspoons.

(g) Because of the large number of drug names in use, care should be taken to avoid misinterpretation. Names should be written clearly and the use of abbreviations for names of drugs and preparations should be avoided. When there is a chance that the drug name may be confused with a similar looking or sounding name, include the purpose of the drug in the prescription. Errors due to similar names are not uncommon. "Elavil" has been dispensed for "Equanil", and "aminophylline" for "amitryptyline."

(h) Never write the instruction "take as directed". Often, patients fail to understand the instructions given in the prescriber's office, or forget the instructions shortly after leaving the office. Similarly, most third party payers will only reimburse the patient or pharmacist for a specific number of doses or duration of treatment. Since "take as directed" fails to provide this informa-

tion, reimbursement may be refused. Some prescription plans may even refuse to reimburse for prescriptions for drugs to be taken "as needed".

(i) Complete all the information on the prescription blank, including the patient's age and address. This information may, or may not be required under state or local regulations, or may be required for controlled drugs but not for other classes of drugs. Because these regulations may be inordinately complex, it is always better to provide all possible information than to run the risk that the prescription will be rejected because of a technical failing. This is doubly essential for prescribers who practice near state borders, since a prescription which is valid in one state may be unacceptable in the state where it is presented for filling.

PATIENT INFORMATION. It has become increasingly common to provide patients with detailed information about the effects, and possible adverse effects of the medications prescribed. Patient package inserts are required for estrogen containing drugs, including the oral contraceptives, and recommendations for information to be provided to patients have been prepared by the American Medical Association, the United States Pharmacopoeia, and many individual regional medical associations and hospitals. In addition, many books have been written for the layman on the effects of drugs and how they should be taken. While the trend towards keeping the patient informed of the nature, and possible effects of drug therapy has been generally beneficial, not all prescribers will agree with specific recommendations provided to the patient. Prescribers should familiarize themselves with the recommendations of at least one of the national patient information services, and the one used by the hospital where they most often practice. Subjects which are open to argument should be discussed with the patient at the time of prescribing, not afterwards.

Quantities of Preparations

The following list indicates the quantities of preparations suitable for various purposes.

Liquid Preparations

Adult Mixtures (10-ml dose)	200 ml (20 doses) 300 ml (30 doses)
Elixirs, Syrups, and Pediatric Mixtures (5-ml dose)	50 ml (10 doses) 100 ml (20 doses) 150 ml (30 doses)
Ear drops, Eye drops, and Nasal Drops	10 ml
Eye Lotions, Gargles, and Mouthwashes	200 ml
Inhalations and Sprays	25 ml
Liniments	100 ml

Dermatological Preparations

	Creams and Ointments	*Lotions*
Face	5 to 15 g	100 ml
Both hands	25 to 50 g	200 ml
Scalp	50 to 100 g	200 ml
Both arms or both legs	100 to 200 g	200 ml
Body	200 g	500 ml
Groins and genitalia	15 to 25 g	100 ml
Dusting powders	50 to 100 g	
Paints	10 to 25 ml	

Approximate Conversions and Units

lb	*kg*	*lbs*	*kg*	*ml*	*fl. oz (approx)*
1	0.45	15	5.8	50	1.8
2	0.91	20	9.1	100	3.5
3	1.36	30	13.6	150	5.3
4	1.81	40	18.2	200	7.0
5	2.27	50	22.7	500	17.6
6	2.72	60	27.2	1000	35.2
7	3.18	70	31.8		
8	3.63	80	36.4		
9	4.08	90	40.9		
10	4.54	100	45.4		
11	4.99	110	50.0		
12	5.44	120	54.5		
13	5.90	130	59.1		
14	6.35	140	63.6		
		150	68.2		

Mass

1 kilogram (kg)	= 1000 grams
1 gram (g)	= 1000 milligrams
1 milligram (mg)	= 1000 micrograms
1 microgram (μg)	= 1000 nanograms
1 nanogram (ng)	= 1000 picograms (pg)

Volume

1 liter	= 1000 milliliters (ml)
1 milliliter	= 1000 microliters (μl)
1 pint	= 473.12 ml

Other units

1 kilocalorie (kcal)	= 4186.8 joules (J)
1000 kilocalories (kcal)	= 4.1868 megajoules (MJ)
1 megajoule (MJ)	= 238.8 kilocalories (kcal)
1 millimeter of mercury (mm Hg)	= 133.3 pascals (Pa)
1 kilopascal (kPa)	= 7.5 mm Hg (pressure)

Prescribing for Children

Children differ from adults in their response to drugs. The first 30 days of life (neonate) is the most dangerous period and dosage must be calculated carefully. In neonates, the toxicity of drugs may be increased by delayed excretion, inefficient renal filtration, differing target organ sensitivity, inadequate detoxifying systems, and enzyme deficiencies.

Prescriptions should state the dose, frequency of administration, and age of the child.

It is particularly important that the strengths of capsules or tablets be stated. Liquid preparations are particularly suitable for young children. However most liquid medicines for children contain sucrose and such medicines have been shown to cause dental caries when taken over a long period. Tablets, or liquid medicines that do not contain sugars, should be used when possible.

When a prescription for a mixture is written for a child, if the dose ordered is smaller than 5 ml the preparation will normally be diluted with a suitable vehicle (such as syrup) so that the required dose is contained in 5 ml. The parent must be instructed to use a standard medicinal spoon to measure the dose and not to heap up a viscous preparation.

Parents should also be advised not to add the dose of any medicine to the milk in the infant's feeding bottle or any other liquid contained in the feeder, since the drug may interact with the milk or liquid or the dosage may be reduced because not all the contents may be drunk.

Parents must also be warned to keep all medicines out of the reach of children in a safe locked place and no medicine should be left in a child's room. They should be advised to dispose of unused medicines by flushing them down a sink or toilet. As an additional precaution, certain medicines may be supplied in child-resistant containers.

Dosage in Children

Pediatric doses are stated in the individual drug entries as far as possible, except where pediatric use is not recommended, as with tetracyclines up to the age of 8 years, or where there are special hazards.

Doses are generally based on the following age ranges:

first month (neonate)
up to 1 year (infant)
1–5 years
6–12 years

Where a single dose is quoted for a given range, it applies to the middle of the age range and extrapolation is necessary to obtain doses for ages at the lower and upper limits.

DOSE CALCULATION. Children's doses may be calculated from age, body-weight, or body-surface area. The most reliable methods are those based on body-surface or body-weight.

Age-related dosage may still be used as a convenient basis for commonly prescribed drugs with a high therapeutic index. The table below may be used to calculate the percentage adult dose using age and weight.

Body-weight can be used to calculate an approximate dose bearing in mind that young children may require a higher dose per kilogram body weight than adults because of their higher metabolic rates. An approximate dose may be calculated from the formula

$$\frac{\text{Patient's weight in kg}}{70} \times \text{adult dose}$$

or

$$\frac{\text{Patient's weight in lb}}{150} \times \text{adult dose}$$

Certain problems may arise if the only criterion used for calculating pediatric dosage is body-weight. A common problem is the obese child who is overweight for his age and height. Calculation by body-weight would result in a much larger dose being given than is really required. In such cases, therefore, doses should be calculated from an ideal weight obtained from a table relating height and age. Where new or potentially toxic drugs are used, the manufacturers' recommended doses should be carefully followed.

Age	Ideal body-weight kg	Ideal body-weight lb	Height mm	Height in	Body-surface m^2	Percentage of adult dose
Newborn*	3.4	7.5	500	20	0.23	12.5
1 month*	4.2	9	550	22	0.26	14.5
3 months*	5.6	12	590	23	0.32	18
6 months	7.7	17	670	26	0.40	22
1 year	10	22	760	30	0.47	25
3 years	14	31	940	37	0.62	33
7 years	23	51	1200	47	0.88	50
12 years	37	81	1480	58	1.25	75
Adult						
Male	68	150	1727	68	1.8	100
Female	56	123	1626	64	1.6	100

* The figures relate to full term and not preterm infants who may need reduced dosage according to their clinical condition.

Body-surface measurements are more accurate for calculation of pediatric doses than body-weight since many physical phenomena are more closely related to body-surface area. The average body-surface area of a 70-kilogram adult is about 1.73 m^2. Thus, to calculate the dose for a child the following formula may be used:

$$\text{Approximate dose for patient} = \frac{\text{surface area of patient } (m^2)}{1.73} \times \text{adult dose}$$

The formula provides only an approximate dose and is unreliable when applied to pre-term infants.

Prescribing for the Elderly

As a group, old people are the largest consumers of medicines. While being potentially the greatest beneficiaries from modern drugs, carefully and rationally prescribed, they are also highly vulnerable to adverse reactions.

Elderly patients are apt to receive multiple drugs for their multiple diseases. They also commonly present with vague symptoms such as headache, sleeplessness, and lightheadedness which may be associated with social stress, as in widowhood, loneliness and family dispersal. The use of drugs for such psychosomatic conditions can at best be a poor substitute for effective social measures and at worst pose a serious threat from adverse reactions.

In very old patients, manifestations of normal aging may be mistaken for disease and inappropriate drugs prescribed. A common misuse of drugs occurs where old people are prescribed drugs, such as prochlorperazine, which are effective in Ménière's disease because they complain of vague giddiness as their postural control is impaired. There is no possibility of benefit from such treatment and the patient may experience serious side effects such as drug-induced parkinsonism, postural hypotension (with falls and fractures), and mental confusion.

Further difficulties may arise in old people who take non-prescribed medicines such as aspirin-containing mixtures and an often bewildering variety of laxatives. It may be quite difficult to establish exactly what the patient is taking.

PHARMACOLOGICAL CONSIDERATIONS. The aging nervous system shows increased *sensitivity* to many commonly used drugs, for example opium alkaloids, many sedatives and tranquilizers, and anti-parkinsonism drugs.

The speed and degree of drug absorption, as well as drug metabolism and excretion, may all be altered in old age. This will often prolong the retention of a drug in the body and may increase plasma half-life by as much as 50%.

By far the most important factor affecting *drug concentration* in the body is the decrease in renal clearance which declines from early adulthood onwards. This must inevitably reduce the rate of drug elimination since most drugs are excreted via the kidney. There is also evidence that the liver's ability to metabolize drugs decreases with old age.

Reduction in plasma albumin concentrations (and reduced plasma binding) occurs commonly in sick old people and may increase the concentration of unbound bioavailable drug. There is little evidence to suggest that drug absorption is significantly altered in old age but drug distribution may be altered by the reduction in body water and increased fat which occurs with aging.

The net result of all these changes is that a given dose in an aged patient will produce higher plasma or tissue concentrations over longer periods of time. Old people are more likely to receive several drugs simultaneously and the dangers of drug interactions are increased.

DOSAGE. First one must always pose the question of whether a drug is indicated at all. Where a placebo effect is necessary, it is essential to use a genuinely inert substance and the temptation to prescribe a 'mild psychotropic' in the vague hope that it might provide additional symptomatic relief must be resisted.

When prescribing drugs in the elderly, it is a sensible policy to limit the range of drugs used to a minimum so that the prescriber may familiarize himself more thoroughly with their doses and side effects in elderly patients.

It is good practice to initiate treatment in aged patients with doses of little more than half that recommended for younger subjects. Pediatric formulations may be useful in allowing greater flexibility of dose.

A system of regular review should be instituted in patients on repeat prescriptions since they may no longer require the medicine or their needs may change from time to time. The correct maintenance dose of a drug may be difficult to establish but is generally significantly lower than for younger patients. It should also be remembered that episodes of acute intercurrent illness, such as myocardial infarction or respiratory-tract infection, may lead to rapid reduction in renal clearance, especially when dehydration supervenes. In these circumstances continuing the usual therapeutic dose of a drug such as digoxin may constitute a toxicity hazard.

COMMON ADVERSE REACTIONS. Adverse reactions often present in the elderly in a vague and nonspecific fashion. Often *mental confusion* presents as the common denominator. Other common manifestations are *constipation* (as with anticholinergics and many tranquilizers) and postural *hypotension* (as with diuretics and many psychotropics).

Hypnotics in common use are responsible for many adverse reactions in the elderly as many of them have plasma half-lives of 30 or more hours. Hence patients may have marked hangover effects throughout the day, with drowsiness, unsteady gait, and sometimes slurred speech and confusion. Prescribers should therefore ascertain the half-lives of the hypnotics they use and should be prepared to switch to those with a shorter action (see section 4.1.1).

Diuretics cause the greatest absolute number of adverse reactions because they are so widely prescribed. They are often used in conditions where drug treatment is unnecessary. For example, they are commonly used to treat simple gravitational edema and this, in most instances, may be relieved in a more physiological manner by encouraging movement, raising the legs, and supplying support stockings.

The following groups are associated with the greatest risk of adverse reactions in old age: drugs used in parkinsonism, antihypertensives, psychotropics, digoxin, hypnotics, and diuretics.

PATIENT COMPLIANCE. At all ages poor compliance with the prescriber's instructions presents a threat to safe treatment and it is obvious that the danger is greater in old patients who have memory impairment, poor eyesight, and difficulty in coping with complex drug regimens. Several rules apply:

(a) determine whether the patient is capable of understanding and remembering the prescriber's instructions. If not, the help of a third party is essential. This person is usually a relative but may be a neighbor, home health aid, or a visiting nurse;
(b) ensure that prescriptions and containers are clearly and explicitly marked with the prescriber's instructions and dose, even for repeat prescriptions. Avoid expressions like 'as directed'. Containers must also be capable of being opened by the patient and it may be necessary to ask the pharmacist to avoid dispensing drugs in child-resistant containers;
(c) simplify drug regimens as far as possible.

Problems associated with imperfect compliance are already formidable and bound to increase. A recent study showed that 25% of old people were taking drugs which had not been recorded as 'current medication' by their general practitioner. Members of primary health care teams should recognize this problem and seek to reduce the dangers including those associated with the uncritical use of repeat prescriptions.

Prescribing in Liver Disease

Liver disease may alter the response to drugs in several ways as indicated below and drug prescribing should be kept to a minimum in all patients with severe liver disease. The Table may be used as a guide to treatment of patients with impaired liver function but is not exhaustive as drugs are included only when there is sufficient information available to provide treatment guidelines.

IMPAIRED DRUG METABOLISM. Metabolism by the liver is the main route of elimination for many drugs, but the hepatic reserve appears to be large and liver disease has to be severe before important changes in drug metabolism occur. Routine liver-function tests are a poor guide to the capacity of the liver to metabolize drugs, and in the individual patient it is not possible to predict the extent to which the metabolism of a particular drug may be impaired.

A few drugs, for example rifampin, are excreted in the bile unchanged and may accumulate in patients with cholestatic jaundice.

HYPOPROTEINEMIA. The hypoalbuminemia in severe liver disease is associated with reduced protein binding and increased toxicity of some highly protein-bound drugs such as phenytoin and prednisone.

REDUCED CLOTTING. Reduced hepatic synthesis of blood-clotting factors, indicated by a prolonged prothrombin time, increases the sensitivity to oral anticoagulants such as warfarin.

HEPATIC ENCEPHALOPATHY. In severe liver disease many drugs can further impair cerebral function and may precipitate hepatic encephalopathy. These include all sedative drugs, narcotic analgesics, and those diuretics that produce hypokalemia.

FLUID OVERLOAD. Edema and ascites in chronic liver disease may be exacerbated by drugs that give rise to fluid retention. These include anti-inflammatory analgesics such as phenylbutazone and indomethacin, and corticosteroids and corticotropin.

HEPATOTOXIC DRUGS. Hepatotoxicity is either dose-related or unpredictable (idiosyncratic). Drugs causing dose-related toxicity may do so at lower doses than in patients with normal liver function, and some drugs producing reactions of the idiosyncratic kind do so more frequently in patients with liver disease. These drugs should be avoided.

Table: Drugs to be avoided or used with caution in liver disease

Drugs	Comment	Drugs	Comment
1: Gastrointestinal system			
Antacids	In patients with fluid retention, avoid those containing large amounts of sodium, e.g. magnesium trisilicate mixture, Gaviscon. Avoid those causing constipation, e.g. calcium compounds, as this can precipitate coma	Cimetidine	Occasional risk of confusional states in patients with liver disease
		Chenodiol (chenodeoxycholic acid)	Avoid in patients with chronic liver disease. Patients with a non-functioning gallbladder do not respond
Antiemetics—see 4		Codeine—see 4 (Narcotic analgesics)	
		Diphenoxylate	May precipitate coma