Healthcare professionals and society in general harbor ambivalent beliefs about drug therapy. Most of us anticipate that drugs will eventually cure or prevent diseases. On the other hand, there is a growing unease about the hazards of medications, which range from minor discomforts that diminish quality of life to life-threatening toxicity. Some clinicians and patients have responded to these threats with a nihilistic attitude toward drugs, but most recognize that rational drug therapy requires weighing the relative risks and benefits of each drug for the individual patient. It is inappropriate to prescribe medications for each symptom presented by the elderly and similarly irrational to deny the benefits of therapy to an individual merely because of advanced age.

Inadequate research in geriatric pharmacology has resulted in serious limitations in the data base needed for making clinical decisions about the relative risks and benefits of drug therapy for the elderly. Despite the observation that the elderly are often the beneficiaries (or victims) of new pharmacologic agents and drug studies, the majority of research has been done on populations over 75 years of age. Even less common are subjects over 75 years of age, although gerontologists and pharmacologists now recognize that responses to medications are most likely to be altered in this "old-old" population. The purposes of this article are to survey the current state of knowledge in geriatric pharmacology and to anticipate, based upon current issues and trends over the past 10 years, the scientific and technological advances likely to promote improved drug therapy for the elderly in the next decade.

ASSESSING BENEFITS

It is important, but often difficult, to distinguish between normal aging effects and the manifestations of disease, since medication may be of benefit in disease but cause only risk of adverse effects in its absence. Diagnostic criteria defined in younger populations may result in over-diagnosis of the elderly. For example, if norms for the glucose tolerance test developed in 30-year-olds are applied to 70-year-olds, 50 percent of the elderly are classified as diabetic. Yet there is currently little evidence to support the notion that vigorous control of blood glucose in the elderly will delay or prevent lethal sequelae such as renal failure, as such action might in young diabetics (Davidson, 1982).

Indeed, attempts to normalize blood glucose in older patients are dangerous since their blunted response to hypoglycemia (like epinephrine released during stress) may mask the warning signs of hypoglycemia. Similar problems arise in defining and treating hyperension in the elderly. While several studies indicate that patients in younger populations benefit from treatment, a recent study of 155 subjects over 80 years of age suggests no reduction in cardiovascular morbidity accruing from treatment of hypertension (Amer et al., 1986).

Extrapolating information about the benefits of drug therapy for the elderly from studies can be misleading, as exemplified by a study of lidocaine for prevention and treatment of ventricular fibrillation. Drug studies show that they are two to seven times more likely to experience adverse drug effects than are younger patients (Hurwitz, 1969; Siedl et al., 1966; Williamson and Chopin, 1980). Because homeostatic mechanisms respond slowly and are less compensatory in older adults, an adverse drug reaction that would be a minor inconvenience to a young adult could prove catastrophic for an elderly patient (Gerber, 1962; several factors contribute to the higher incidence of adverse drug effects in the elderly, the most important of which is polypharmacy, or exposure to multiple drugs, that occurs in many elderly patients). Unfortunated, these conclusions were buried in the text of the report and would not have been apparent to the clinician who read only the abstract.

Elderly patients often present with atypical signs and symptoms of disease, leading to incorrect diagnosis and treatment aimed at the wrong disease. Non-specific symptoms such as poor appetite, falling, incontinence, dizziness, acute confusion, and weight loss may be manifestations of diseases as diverse as anemia, pneumonia, acute cholecystitis, and myocardial infarction. Failure to respond to drug therapy or drug toxicity may be harbinger of misdiagnosis rather than medication failure (Ouslander, 1981).

The number of studies addressing the manifestations of disease in the elderly and controlled trials to determine the effects of drug treatment on morbidity and mortality in this population is steadily increasing. Although deficits in the research base necessary to assess the benefits of drug therapy will persist, clinicians will increasingly be challenged to keep abreast of relevant clinical decision-making.

ASSESSING RISKS

Although the elderly may be less likely to report adverse drug effects unless specifically questioned, studies show that they are two to seven times more likely to experience an adverse drug effect than are younger adults (Hurwitz, 1969; Siedl et al., 1966; Williamson and Chopin, 1980). Because homeostatic mechanisms respond slowly and are less compensatory in older adults, an adverse drug reaction that would be a minor inconvenience to a young adult could prove catastrophic for an elderly patient (Gerber, 1962). Several factors contribute to the higher incidence of adverse drug effects in the elderly, the most important of which is polypharmacy, or exposure to multiple drugs, that occurs in many elderly patients. Unless specifically questioned, studies show that they are two to seven times more likely to experience an adverse drug effect than are younger adults (Hurwitz, 1969; Siedl et al., 1966; Williamson and Chopin, 1980). Because homeostatic mechanisms respond slowly and are less compensatory in older adults, an adverse drug reaction that would be a minor inconvenience to a young adult could prove catastrophic for an elderly patient (Gerber, 1962). Several factors contribute to the higher incidence of adverse drug effects in the elderly, the most important of which is polypharmacy, or exposure to multiple drugs, that occurs in many elderly patients. Unfortunated, these conclusions were buried in the text of the report and would not have been apparent to the clinician who read only the abstract.

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multiple agents (Williamson, 1980). In addition, drugs may complicate age-related physiologic and neuropsychiatric changes and increase susceptibility to adverse outcome among the elderly.

Anticholinergic (atropine-like) drugs exacerbate these problems. Over 800 prescription and nonprescription products marketed in the United States, including antihistamines, antidepressants, and antispasmodics, have anticholinergic properties. Studies indicate that between 30 percent and 60 percent of nursing home patients receive anticholinergic drugs, and up to 30 percent simultaneously receive two or more such agents (Blazer et al., 1989; Pepperc, 1985; Sedorf et al., 1985). Anticholinergic effects include memory impairment, confusion, ataxia (impaired ability to coordinate movement), dry mouth, urinary hesitancy and retention (especially in men with prostatic enlargement), and constipation. The severity of some of these effects is evident—for example, urinary retention, which can lead to renal damage—but some of the effects are less obvious, for example, inability to maintain body temperature during this period. Cognitive functioning in this group (Davies and Maloney, 1976; Sanny, 1984). One study (Pepperc, 1985) suggested that use of drugs with anticholinergic activity increases postural sway, which has been linked prospectively and retrospectively to falls in the elderly (Overslaaij et al., 1977; Overslaaij, 1980; Shulman, 1983).

Recognition of physiologic alterations of aging can aid identification of preventable complications of medications. Lipitz and associates (1983) noted postprandial orthostatic hypotension (at times be appropriate (Cooper et al., 1982). In summary, the potential risks of drug therapy in the elderly are diverse and complex, ranging from side-effects to drug interactions and noncompliance. Much remains uncertain about the incidence of specific adverse drug effects and effective methods to minimize these risks. Further, studies have not consistently documented that decreasing the number of medications, patient education, or memory aids improve outcome.
pliances in the elderly (Gorman et al., 1982). Until there are consistency and rigor in the definition and measurement of adverse drug effects, of compliance, and of clinically significant drug interactions, divergent conclusions will continue to characterize research on this aspect of geriatric pharmacology.

**Drug Disposition**

Research in geriatric pharmacology is best established in the speciality of pharmacokinetics (disposition of drug in the body). Progress in this area over the past decade has been remarkable, and this trend is likely to continue with the implementation of proposed Food and Drug Administration guidelines for clinical evaluation of drugs being developed for use in the elderly. In the early 1970s, the state of knowledge about pharmacokinetics and pharmacodynamics (action of drug on the body) consisted primarily of the following findings: that most drugs tested had prolonged half-lives in the elderly, a deduction that renal clearance of drugs was reduced, a suspicion that the elderly were more sensitive to many agents, and evidence that the elderly demonstrated an incredible amount of diversity in all aspects of pharmacology. There was little guidance that could be offered the clinician except the warning to "start low and go slow" under the presumption that prolonged drug half-life always required reduced loading and maintenance doses.

Over the past decade much of the variance in the response of the elderly to medications has been explained, but it is still evident that older people are as diverse in pharmacologic parameters as they are in other physiologic and neuropsychiatric functions. Age-related changes are thought to be significant in altered drug response have proven unimportant. For example, during aging there are many physiologic changes of the gastrointestinal tract that theoretically could alter drug absorption, but no clinically significant alterations in absorption have been identified in the elderly, except when there is congestive heart failure. Increased liver weight is due to the increased volume of distribution, which improves solubility, which is often less than was required with younger dosage forms. In addition, there are fewer problems related to comitant disease or drug therapy, such as anemia (Greenblatt et al., 1982).

Similarly, decreased serum albumin concentration that occurs in aging and results in significant decrease in the ratio of bound to free (active) drug has frequently been cited in explanation for increased drug response. However, since both the clearance and effects of drugs are related to the free-drug concentration, the steady-state (homeostatic) balance, within the body) effects and maintenance dose regimen should not be altered by serum albumin changes alone. Serum albumin is also decreased drug elimination (Gerber, 1982; Katzung, 1987). Altered albumin binding may explain increased susceptibility to drug interactions resulting from competition for protein binding and may also alter loading dose and the interpretation of laboratory determinations of blood levels of drugs. When interpreting blood levels of highly albumin-bound drugs which generally reconstitute both bound and free fractions of the drug, consideration must be given to the fact that lower levels may be therapeutically significant, since there is a higher ratio of free drug.

Early findings of prolonged half-lives of drugs in the elderly offered little guidance to selecting drug dosage, since both increased volume of distribution and decreased clearance result in prolonged half-life. However, volume of distribution affects the loading dose, while clearance determines the maintenance dose, so the clinical implications of prolonged half-life depend upon the parameter altered by the aging process. For example, the increase in geriatric half-life common among the elderly is due predominantly to decreased clearance, so the weight-adjusted loading dose is the same for younger and older patients, but the maintenance dose often must be smaller for older patients (Gerber, 1982).

The distribution characteristics of drugs are altered by aging. Most common is the fact that the elderly are usually smaller than younger patients. Further, in aging there is a shift in body composition, with an increase in fat mass and a decrease in lean mass. Par-soluble drugs have larger volumes of distribution in the elderly, requiring larger relative loading doses, and are slower to approximate steady-state (Jennings et al., 1985). For example, most of the increased average half-life of diazepam, from 20 hours in young adults to 80 hours in elderly adults, is due to the increased volume of distribution. This explains a frequent clinical phenomenon where the elderly patient, whose anxiety or agitation was poorly controlled during the initial days of therapy, becomes somnolent after a week or more on diazepam or other central nervous system depressant drug. As blood levels continue to rise until the drug approximates steady state (four to five half-lives), and the diazepam will not reach steady state for 50 to 400 hours, the full clinical impact of such drugs may be delayed.

Metabolic clearance of some drugs changes with aging, while metabolism of many drugs is unaffected. However, the decrements in renal function are so consistent among the elderly that any drug eliminated greater than 20 percent unchanged (active) in the urine should probably be administered in lower initial maintenance dosages in the elderly.

It is now recognized that most of the apparent changes in sensitivity of the elderly to drugs are due to pharmacokinetic changes and diminished homeostatic responses. However, studies have documented decreased responsiveness to drugs that work at the beta-adrenergic receptor, including beta stimulants and beta blockers (Vesell et al., 1979). These decrements have been linked to receptor-effector coupling rather than to altered receptor function; however, the increased incidence of bleeding noted with anticoagulant therapy in elderly patients is attributed more to diminished capacity of degenerated vessels to achieve mechanical hemostasis, a homeostatic response, rather than to increased receptor sensitivity.

New dosage forms. Technological advances in drug delivery systems offer less frequent dosing, more consistent blood levels, and fewer adverse effects because the total dosage is often less than was required with older dosage forms. In addition, there are fewer problems related to concomitant disease and drug therapy. These advantages may decrease noncompliance and provide improved disease control. Examples of these new systems include liquid digoxin in gelatin capsules, in which improved solubility provides about 25 percent increased bioavailability and possibly more consistent absorption. Coating...
drugs with waxes, cellulose films, and polymers that result in a predetermined rate over an extended period (controlled release) has resulted in a group of drugs currently available orally for amitriptyline, scopolamine, estrogen, and others. (Maierhofer, 1985; Pepper, 1986).

Phospholipid vesicles called liposomes are proposed for the future as transdermal drug delivery systems often deliver reduced toxicity and adverse reactions compared to traditional systemic administration. The enhanced uptake over the administered drug dosage between the skin and the systemic circulation is another problem amenable to a team approach, especially if the patient is a participant. Commonly overlooked is an effective way to assess compliance is to ask the patient; the patient will generally explain not only whether he or she is taking the drug as ordered but also the reason for any noncompliance. Improving drug therapy is a complex objective, achievable through coordinated effort.

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RECOMMENDATIONS

While the knowledge base regarding pharmacy in the elderly has expanded over the last decade and will undoubtedly increase rapidly in the future, the fact remains that the most consistent characteristic of the elderly is diversity. For each patient there is a unique set of biologic, pathologic, and psychosocial factors affecting drug response and requiring an individualized approach. For example, although renal function declines at an average of 50 percent between ages of 20 and 80, some 80-year-olds have "normal" creatinine clearance and would not be expected to respond to reduced dosages of drugs.

Improving drug therapy for the elderly is increasingly a multidisciplinary responsibility. The pharmacist (physician, dentist, podiatrist, nurse practitioner, and the like) has the responsibility of identifying drug therapy, drug selection, and communication of the prescribed drug regimen to other members of the healthcare team, including the patient. Through awareness of the specific desired outcome of each drug, all members of the team can apply their unique skills to promote optimal drug therapy. The patient is a critical part of this recognition where the risks outweigh the achieved or desired outcomes, and to propose nonpharmacologic alternatives if appropriate.

Clinical pharmacists have demonstrated important contributions through identification of clinically significant drug interactions and consultation on drug selection. While it is widely accepted that the safer way to prescribe for the elderly is to start with small doses and titrate (move up slowly so the desired response is achieved with the smallest amount of substance necessary) ("start low and go slow"), hospitalizations are usually too short to complete the titration, and the frequent returns to clinic or office for monitoring may constitute a problem for patient and prescriber. In many settings, such as the home, nursing homes, and clinics, nurses have assumed the responsibility for monitoring and titrating drug dosages within the goals and protocols established by the prescriber. Noncompliance is another problem amenable to a team approach, especially if the patient is a participant. Commonly overlooked is an effective way to assess compliance is to ask the patient; the patient will generally explain not only whether he or she is taking the drug as ordered but also the reason for any noncompliance. Improving drug therapy is a complex objective, achievable through coordinated effort.

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Innovations in Homecare

The recent growth in home healthcare has been coupled with phenomenal developments in technology and major changes in society's attitudes toward illness and death.

by JOAN E. CUMMINGS

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The insitute desire to re-
main in one's own home can result in the freedom, dignity, and comfort that accompanies independent living. Pa-
tient acceptance of and desire for homecare as an alternative to institutional care is well known, as is the general attitude among the public and healthcare professionals that nursing homes, however well run, are places of last resort. The tendency for patients to receive more care at home has been increasing and is ac-
companied by a high degree of satis-
faction, but enthusiasm has been tem-
pered by concern over availability of resources in the community to pro-
vide the necessary support (both medical and social).

As longevity increases and our medical technology provides at least partial control of some serious ill-
nesses, the complexity of care re-
quired for optimal functioning of the individual also increases. When the goal is independent living and home-
care is considered as an alternative to nur-
ing home care, or as a way to avoid premature nursing home place-
ment, then the support services re-
quired encompass a broad contin-
uum of types of care and include social support as well as healthcare.

To add to the problem, societal is-

sues of cost containment, individual rights, personal dignity and freedom of choicet, and access to healthcare of-
ten produce conflicting public policy, legislation, and regulations. For ex-

ample, efforts at containment of hos-
pital costs utilizing prospective re-
imbursment (diagnosis-related groups, or DRGs) have provided ma-

jor motivation for earlier discharge of pa-

tients. As a result, many of these pa-
tients may have significant needs for homecare in order to either make a successful recovery from illness or ma-

ximize potential for remaining at home. However, these needs arise as cost-containment policies are also ad-

versely affecting access to increased amounts of homecare.

Looking at the growth of the el-
derly in our population, with their in-
creased disability (46 percent of those over the age of 75 have major limita-
tions in their abilities to perform ac-
tivities of daily living) (U.S. Senate, 1984), the need for maintenance care for chronic illness is apparent. How-

ever, the current system, with Medi-
care as the prototype, still has much of its focus on the provision of acute care, whether at home or in an insti-

tution. Current reimbursement meth-

ods that dictate types and amounts of homecare, set spending-caps, and re-

quired multiple funding sources have all hindered the development of a co-

hesive, coordinated system for the provision of long-term care.

It is in this setting that homecare has undergone tremendous growth, development, and change over the 25 years since the introduction of Medi-
care. The increases that have oc-
curred can be grouped into three broad areas: medical technology (in-


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