Geriatric Drug Therapy

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Elderly Americans make up 11 percent of the population but consume 25 percent of all prescription medications. The incidence of adverse drug effects is 1.5 to 3 times higher in older patients and accounts for numerous hospitalizations. The basic pharmacokinetic parameters of absorption, distribution, metabolism, and excretion are all significantly altered in geriatric patients. Certain specific drug side effects, such as orthostatic hypotension and anticholinergic effects, can be particularly hazardous in older patients. This paper describes general therapeutic principles for geriatric patients. Commonly used drug categories are considered separately. A thorough knowledge of these principles will allow the physician to prescribe drugs more effectively, improve patient compliance, and minimize adverse drug effects.

From 1900 to 1980, the life expectancy of the average American increased from 47 to 73 years. Recent statistics reveal that the life expectancy of a white female in this country is 77 years and the life expectancy of a white man is 70 years. The tremendous increase in life expectancy since the turn of the century is largely related to improved obstetrical and neonatal care, the advent of effective antibiotics, and successful public health programs. Although the life expectancy from birth has increased dramatically since 1900, the life expectancy of a 65-year-old person has increased only 2.9 years. The major causes of morbidity and mortality are no longer acute disease processes, but rather are chronic diseases such as hypertension, coronary artery disease, chronic obstructive pulmonary disease, and congestive heart failure. It has been estimated that eradication of heart disease and stroke would increase the average life expectancy by 11 years; eradication of cancer would increase the life expectancy by two years.[1]

Although the life expectancy of Americans has been increasing, the human life span appears to be fixed. Statistical analysis of mortality data reveals that ideal life span is 85 years.[2] The inclusion of two standard deviations yields a range from 77 to 93 years. Thus under ideal conditions, approximately 95 percent of the population would die between these ages. Only 0.01 percent of the population of developed countries live beyond 100 years of age. The oldest documented age is 114 years. There has been no satisfactory evidence that any society has a greater life span than another.

Because of increasing life expectancy, the number of elderly Americans (aged 65 years or over) has been increasing at a rate greater than that of the general population. In 1940 elderly Americans accounted for less than 7 percent of the

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0094-3509/81/110599-11$02.75

total population. This figure increased to 11 percent or 24 million, by 1976. Projections indicate that by 1990 the elderly will make up approximately 13 percent (27.5 million) of the population.

Drug Usage

Approximately one third of the total health care expenditures in this country are consumed by patients 65 years of age and older. Elderly Americans occupy 40 to 50 percent of acute care hospital beds. Older Americans spend $3 billion a year on medications. This accounts for 25 percent of the total expenditures for drugs. At hospital discharge, 25 percent of elderly patients receive prescriptions for six or more drugs. In nursing homes, it is not uncommon for some patients to be receiving 12 to 15 drugs concurrently. The incidence of adverse drug effects increases dramatically with age and the number of medicines prescribed. Elderly patients suffer a rate of adverse drug reactions that is 1.5 to 3 times the normal rate. Patient compliance in the elderly is disturbingly low. It has been estimated that the rate of noncompliance in this age group is 60 percent or more. Many patients omit doses or take extra doses as dictated by their symptoms. It is not uncommon for the patient to take the wrong medication for a particular symptom or to self-medicate with an over-the-counter nonprescribed drug.[3-5]

Physiology of Aging

There have been many theories proposed to explain the process of aging. At a cellular level, several studies have shown that human embryonic fibroblasts and human diploid cells are capable of only a finite number of cell divisions (approximately 50). Other studies have shown numerous biochemical and functional decrements that progressively appear with time.

The most universal characteristic of aging at an organ level is a progressive deterioration of organ reserve. A major function of all organs is to maintain homeostasis. In young healthy adults, the functional capacity of various organs is many times that required to sustain life. Organ reserve allows the human body to compensate for large variations in physiologic parameters. Aging causes a progressive deterioration in organ reserve. Compensatory processes are limited, and biological insults are not tolerated as well. Physiologic parameters that decrease with aging include cardiac output, creatinine clearance, hepatic blood flow, and pulmonary function. Often organ failure occurs at a younger than expected age because of intervening disease processes. For example, hypertension causes a premature decline in cardiac and renal function; chronic bronchitis and emphysema cause a premature decline in pulmonary function.

Altered Pharmacokinetics

Pharmacokinetic parameters are significantly altered in elderly patients. The changes in the way an elderly person handles a drug may not be that important for a drug with a high therapeutic index (ie, penicillin). However, these changes are very important and must be considered for a drug with a low therapeutic index (ie, gentamicin, digoxin, theophylline).

Absorption

The capacity of the parietal cells to secrete acid seems to be diminished in elderly patients; consequently, the gastric pH is significantly higher. This change would tend to decrease the absorption of acidic drugs such as aspirin. Gastric emptying time is reduced; therefore, drugs with a high ulcerogenic potential such as aspirin, indomethacin, and phenylbutazone would be in contact with the gastric mucosa for a longer period of time. Intestinal blood flow is also decreased in elderly patients, a fact which may affect the absorption of some drugs.

Distribution

The proportion of lean body mass to total body weight decreases with age. Digoxin is an example of a drug that distributes well into lean body tissues but does not distribute to any significant degree in adipose tissue. Consequently, a reduction in lean body mass will produce elevated serum digoxin levels when other parameters such as dose and creatinine clearance are held constant. Barbiturates, phenothiazines, and general anesthetics are examples of drugs which distribute well into adipose tissue. Elderly patients have an increased proportion of body fat which can serve as a reservoir for these drugs and prolong their duration of

action. The proportion of total body water and extracellular fluid also declines with age, which can reduce the volume of distribution of some drugs and result in proportionately higher serum drug levels.

The total amount of serum albumin declines with age. Several studies have shown a decline in the range of 15 to 25 percent in patients over 60 years of age. Phenytoin, diazepam, warfarin, digitoxin, and naproxen are examples of drugs highly bound to serum albumin. A reduction in the amount of total serum albumin will result in an increased amount of free (active) drug. Since most drug assays measure both free and bound drug, the serum drug level is not an accurate predictor of free drug when hypoalbuminemia is present. In this situation, a normally therapeutic serum drug level may actually represent a toxic amount of free drug.

Metabolism

Hepatic blood flow declines steadily with age. This is largely related to a decreased cardiac output. In patients with congestive heart failure, hepatic blood flow is even further decreased. The ability of the liver to metabolize many drugs depends on hepatic blood flow. Beta blockers, narcotics, nitrates, hydralazine, and tricyclic antidepressants are examples of drugs that undergo a large "first-pass" metabolism in the liver. This means that a large proportion of the orally administered drug is metabolized before reaching the systemic circulation. Elderly patients metabolize a smaller proportion of these drugs during the "first pass" and subsequently develop higher serum drug levels. Consequently, the usual dose of these drugs should be significantly reduced in older patients.

The capacity of hepatic microsomal enzymes to metabolize certain drugs appears to diminish with age. The mixed function oxidase system (P-450) is largely responsible for the metabolism of numerous drugs, including the benzodiazepines, warfarin, phenytoin, and many others. Hepatic clearance of these drugs is reduced in elderly patients; subsequently, the duration of action is prolonged.[6]

Excretion

Creatinine clearance decreases steadily with age. Renal size, blood flow, and number of functioning glomeruli decrease significantly with age. Because of the decreased lean body mass, the creatinine clearance can be significantly reduced in the presence of a normal serum creatinine. Siersbaek-Nielson measured the creatinine clearance in 149 men of various ages with a normal serum creatinine.[7] The average creatinine clearance (corrected to 1.73 sq m of body surface area) for geriatric age groups was as follows: 60 to 69 years, 72 ml/min; 70 to 79 years, 64 ml/min; 80 to 89 years, 47 ml/min; and 90 to 99 years, 34 ml/min. A method for estimating creatinine clearance from serum creatinine is outlined in Table 1. Because of this progressive decline in creatinine clearance with age, the dose of drugs that are largely dependent on the kidney for excretion (ie, digoxin, gentamicin) must be reduced in elderly patients.[8]

Table 1. Method for Estimating Creatinine Clearance from Serum Creatinine

For Men: $Ccr = \frac{140 - Age}{Scr}$

For Women: $Ccr = \frac{140 - Age}{Scr} \times 0.85$

Ccr=creatinine clearance (corrected to 70 kg body weight)
Scr=serum creatinine

Selected Drug Categories

Anticholinergics

Anticholinergic drugs are prescribed frequently for elderly patients. Examples of anticholinergic drugs and other drugs with prominent anticholinergic side effects are shown in Table 2. These side effects, which can be particularly bothersome, even dangerous, in older patients, typically include confusion, blurred vision, dry mouth, palpitations, urinary retention, and constipation. Elderly patients also appear to be more sensitive to the central nervous sytem side effects of anticholinergic drugs, which can cause psychosis, confusion, disorientation, hallucinations, and delirium. Mental function should be monitored closely when prescribing these drugs.

Blurred vision is caused by pupillary dilatation and paralysis of the ciliary muscle. This can be an annoying side effect in older patients and may lead to motor vehicle accidents and falls. Anticholin-

Table 2. Drugs With Anticholinergic Effects

Therapeutic Classification	Example
Antispasmotics	Belladonna alkaloids (atropine, hyoscyamine); dicyclomine (Bentyl); propantheline (Pro-Banthine)
Antiparkinsonian drugs	Benztropine (Cogentin); trihexyphenidyl (Artane)
Antihistamines	Diphenhydramine (Benadryl); chlorpheniramine (Chlor-Trimeton)
Tricyclic antidepressants	Amitriptyline (Elavil); imipramine (Tofranil)
Antiarrhythmics	Quinidine; disopyramide (Norpace)
Phenothiazine tranquilizers	Chlorpromazine (Thorazine)

ergic drugs can also precipitate or aggravate narrow angle glaucoma. These drugs tend to reduce bronchial secretions as well, which can cause decreased expectoration and mucous plugging. This can lead to a deterioration in pulmonary function in patients with chronic bronchitis, emphysema, and asthma. The tachycardia caused by anticholinergic drugs can be dangerous in patients with congestive heart failure, coronary artery disease, and cardiac arrhythmias. Reduced bladder tone can be particularly bothersome in a patient with prostatic hypertrophy and can lead to acute urinary retention in some patients.

When anticholinergic drugs are indicated in elderly patients, initial small doses should be prescribed and the patient should be monitored closely for side effects. Anticholinergics should not be prescribed routinely to all patients receiving phenothiazine tranquilizers to prevent extrapyramidal reactions. Should an extrapyramidal reaction develop, the drugs can be prescribed but should not be continued indefinitely. In an elderly patient with extrapyramidal reactions who is unable to tolerate an anticholinergic drug, amantadine (Symmetrel) may be tried.

Antiadrenergics

Reserpine, clonidine (Catapres), and methyldopa (Aldomet) can all cause sedation and depression. These drugs frequently cause orthostatic hypotension, which can be a dangerous side effect in elderly patients who have significantly compromised vascular beds and are unable to adequately increase their cardiac output. Clonidine should not be discontinued abruptly because of the risk of rebound hypertension.

Currently available beta-adrenergic blocking drugs include propranolol (Inderal), metoprolol (Lopressor), and naldolol (Corgard). Since these drugs undergo large first-pass metabolism, the dose should be reduced in older patients. Elderly patients should also be monitored closely for signs of left ventricular dysfunction and early congestive heart failure. Although metoprolol is a selective $beta_1$ blocking drug, it cannot be used with impunity in patients with asthma or chronic obstructive pulmonary disease. The drug becomes a nonselective beta blocker at doses greater than 100 mg.[9] If a beta blocker is indicated in a patient with chronic obstructive pulmonary disease or asthma, metoprolol can be prescribed most safely by using small doses (ie, 50 mg/day) in combination with a $beta_2$ agonist, such as terbutaline.

Naldolol has the advantage of a long half-life, which allows one dose per day and improved patient compliance. However, naldolol is excreted primarily by the kidney, and the dose should be reduced in elderly patients according to renal function.

Sympathomimetics

The administration of a sympathomimetic drug to an elderly patient is associated with increased risk. These drugs may produce serious adverse effects in patients with hypertension, coronary artery disease, and cardiac arrhythmias. In treating an elderly patient with reversible airway obstruction, a $beta_2$ agonist is preferred. Terbutaline

(Brethine) can be administered subcutaneously, but it has a slower onset of action than epinephrine. Some reports have indicated that subcutaneous terbutaline produces more cardiac stimulation than the oral administration of the drug. Metaproterenol (Alupent) is another $beta_2$ agonist but has the disadvantage of lower bioavailability and shorter duration of action following oral administration. $Beta_2$ agonists available in metered dose inhalers include metaproterenol and albuterol (Ventolin); these drugs are preferable to nonspecific beta agonists, such as isoproterenol (Isuprel).

Xanthine Alkaloids

Theophylline is primarily metabolized by the liver. Significant dosage reductions are required in elderly patients, especially patients with congestive heart failure or hepatic insufficiency.[10] Oral dosage schedules should be calculated on the basis of lean body mass and should be in the range of 7 to 10 mg/kg/day. When aminophylline is indicated for intravenous use, a loading dose of 4 to 6 mg/kg can be infused slowly. The maintenance dose should be reduced by 50 percent in older patients to approximately 0.5 mg/kg/hr. Intravenous aminophylline should be delivered by using an IVAC or Soluset, and the dosage should be adjusted according to serum drug levels.

Vasodilators

Vasodilators are useful in treating a number of clinical problems that occur in elderly patients. Some indications for vasodilator therapy are well accepted; others are controversial. In some clinical situations vasodilator therapy has been proven ineffective. Angina pectoris, hypertension, and refractory congestive heart failure are well-established indications for vasodilator therapy. Nitrates are the vasodilators of choice for the treatment of angina pectoris. These drugs predominantly cause venodilation and venous pooling, which reduces preload. Reflex tachycardia can occur but is more common in younger patients. Because orally administered nitrates undergo a large first-pass metabolism in the liver, the dosage should be significantly reduced in elderly patients or in patients with congestive heart failure. Sublingual nitroglycerin tablets frequently cause cutaneous vasodilation, pounding headache, and in some patients hypotension. Older patients should be warned about these side effects. Nitroglycerin sublingual tablets should be stored in a light resistant, sealed container. The tablets rapidly lose their potency when exposed to the air. Six months after the seal is broken, any remaining tablets should be discarded and a new container purchased. Nitroglycerin ointment is a popular long-acting form of nitroglycerin that can be applied every six to eight hours.[11]

Hydralazine (Apresoline) also undergoes a large first-pass metabolism in the liver; therefore, the usual dosage should be reduced in elderly patients. Reflex tachycardia is a common side effect in patients with normal cardiovascular reflexes. This compensatory reaction can negate the drug's antihypertensive effect and exacerbate the symptoms of coronary artery disease. When hydralazine is used as an afterload reducing agent in patients with refractory congestive heart failure, reflex tachycardia is seldom observed. Drug induced lupus erythematosus is uncommon in patients taking a total daily dose of 200 mg or less.[12]

Prazosin (Minipress), an $alpha_1$ blocking drug, is sometimes prescribed in elderly patients for the treatment of hypertension. Some patients experience a "first-dose syncope" with this drug, which may result in a fall or other accident. Initially, a 1-mg test dose should be given one or two hours before bedtime. The patient should be warned of this side effect and should be instructed to remain in a safe place until this adverse reaction is excluded. Tolerance to the drug's effect occurs when treating refractory congestive heart failure but not hypertension.

Papaverine (Pavabid), niacin, cyclandelate (Cyclospasmol), and isoxsuprine (Vasodilan) are examples of vasodilators that are promoted for the treatment of peripheral vascular and cerebral vascular disease. These drugs have been shown to be ineffective in the treatment of atherosclerotic peripheral vascular disease and may actually cause the shunting of blood away from ischemic vascular beds. On the other hand, these drugs may have some role in the treatment of vasospastic disorders such as Raynaud's phenomenon.[13] There have been numerous studies that have attempted to evaluate the effectiveness of vasodilators in the treatment of senile dementias. The only drug that may be of some benefit in selected patients is dihydroergotoxin (Hydergine). The vasodilating effect of this drug appears to be secondary to an increased rate of neuronal metabolism.[14]

Table 3. Characteristics of Two Cardiac Glycosides

	Digoxin	Digitoxin
Gastrointestinal absorption	75 percent	95—100 percent
Onset of action	15—30 minutes	25—120 minutes
Peak effect	2—5 hours	4—12 hours
Average half-life	36 hours	5 days
Percent bound to albumin	20 percent	97 percent
Major route of elimination	Kidneys	Liver
Average loading dose		
Oral	1.0—1.5 mg	0.7—1.2 mg
Intravenous	0.75—1.0 mg	
Usual maintenance dose	0.125—0.5 mg	0.1 mg
Therapeutic blood level	1.0—1.5 ng/ml	15—25 ng/ml

Diuretics

The most common side effects of diuretic therapy in elderly patients are excessive dehydration and hypokalemia. Hypokalemia may be particularly dangerous in older patients with cardiac arrhythmias and in patients receiving a digitalis glycoside. Potassium loss appears to correlate not only with dose but also with the potency and duration of action of the diuretic. In general, a loop diuretic will produce more potassium loss (per unit time) than a thiazide diuretic; a long-acting thiazide such as chlorthalidone will produce more potassium loss than will a short-acting thiazide such as chlorothiazide. A high intake of dietary sodium also potentiates potassium loss. In treating hypertension, doses in excess of 50 mg/day appear to increase adverse effects significantly without a proportional increase in therapeutic response.

Thiazide diuretics are generally not effective in patients with significant renal insufficiency (creatinine clearance, 50 cc/min or less). Potassium sparing diuretics should be used with caution in patients with significant renal insufficiency, since hyperkalemia may occur. Hyperkalemia may also occur in elderly patients receiving potassium sparing diuretics in conjunction with potassium chloride supplements. The combination of furosemide (Lasix) and metolazone (Diulo, Zaroxolyn) may cause severe electrolyte abnormalities in elderly patients.[15]

Digitalis Glycosides

The digitalis glycosides are a common source of adverse drug effects in elderly patients. A thorough knowledge of the pharmacokinetics of digoxin and digitoxin is required if these drugs are to be prescribed safely. Several pharmacokinetic parameters of digoxin and digitoxin are compared in Table 3. Because the excretion of digoxin is primarily dependent upon renal function, the dose must be significantly reduced in elderly patients. A normal serum creatinine in an elderly patient does not insure normal renal function. Digoxin toxicity can best be avoided by calculating the loading and maintenance dose (Table 4) and by closely monitoring the patient's renal and electrolyte status. Burroughs Wellcome Company has recently revised their drug monograph on Lanoxin. The new monograph provides updated information on the pharmacokinetics of digoxin and several excellent methods for calculating an appropriate dose. The physician should not assume that gastrointestinal side effects will be a harbinger of serious cardiac toxicity. Fifty percent of elderly patients may have significant cardiac toxicity with no gastrointestinal side effects. The pulse rate, electrocardiogram, and serum drug level are also important tools for monitoring digitalis therapy. Digitalis toxicity should be ruled out in any elderly patient with ventricular ectopy.[16]

The co-administration of quinidine with digoxin results in significantly elevated serum digoxin levels (twofold). Whether this increase in serum digoxin corresponds to increased digoxin activity at myocardial receptor sites is being debated. Until more information is available, it would seem prudent to reduce the dose of digoxin when quinidine therapy is instituted and to monitor the patient closely for adverse effects.[17]

Table 4. Calculation of Digoxin Dose

Total body digoxin (TBD) = 10 μg/kg × lean body mass*
(Desired pool)

$$\text{Percent digoxin excreted/day} = 14 + \frac{\text{creatinine clearance}}{5}$$

Maintenance dose (mg/day) = percent excreted (mg/day)

Example: Calculate digoxin loading dose and maintenance dose in a 75-kg (lean mass) male with a creatinine clearance of 50 cc/min

Desired TBD = 10 μg/kg × 75 kg = .75 mg

Loading dose (PO) = 1.0 mg
(75 percent absorption)

$$\text{Percent digoxin excreted/day} = 14 + \frac{50}{5} = 24 \text{ percent}$$

Maintenance dose = 1.0 mg × 24 percent

Maintenance dose = 0.25 mg

*10 μg/kg will provide an adequate therapeutic effect with minimal toxicity in patients with congestive heart failure in normal sinus rhythm. Higher doses (12-15 μg/kg) are often required in patients with atrial fibrillation

Antiarrhythmics

Antiarrhythmic drugs are frequently prescribed in elderly patients. All of these drugs can be hazardous to these patients if not prescribed properly. Quinidine, procainamide (Pronestyl), and disopyramide (Norpace) are all drugs that have significant cardiac depressant properties. This may be a problem in patients with pre-existing left ventricular dysfunction. Disopyramide appears to have the most pronounced cardiac depressant effect.[18] Disopyramide and propranolol (Inderal) are generally not prescribed in combination because of the summation effect of their potent negative ionotropic properties. Other properties of quinidine, procainamide, and disopyramide include prolongation of conduction time and delayed repolarization. The drugs should be used with extreme caution in patients with pre-existing conduction defects. The QRS duration and QT interval should be monitored during therapy. Prolongation of the QRS duration indicates a toxic dose; a prolonged QT interval predisposes the patient to paradoxical ventricular arrhythmias.

Diarrhea is a common and annoying side effect of quinidine therapy which limits patient compliance. The coadministration of an aluminum containing antacid (ie, Amphojel) does not adversely affect absorption and tends to reduce the incidence of quinidine induced diarrhea. Quinidine is largely metabolized by the liver, and the dose should be reduced in elderly patients.

The clinical use of procainamide is frequently limited by the high incidence of drug induced lupus erythematosus. Approximately 90 percent of patients receiving procainamide for one year or more demonstrate positive antinuclear antibodies. Although the drug need not be stopped in asymptomatic patients with positive antinuclear antibodies, symptoms may be vague and difficult to recognize. In addition to the more common symptoms of arthralgias and fever, elderly patients may demonstrate only fatigue or a persistent cough. Drug induced lupus erythematosus has no adverse effects on the kidneys. Procainamide is primarily eliminated by the kidneys. N-acetyl procainamide (NAPA) is an active metabolite that is

exclusively eliminated by the kidneys. The accumulation of NAPA is more likely in elderly patients with renal insufficiency. Although routine serum procainamide levels do not measure NAPA, the concentration of this active metabolite in serum can be measured.

Disopyramide has significant anticholinergic properties, and urinary retention is a common side effect. This is especially true in elderly men with prostatic hypertrophy. Since disopyramide is predominantly excreted by the kidneys, the dosage of this drug should also be reduced in elderly patients.[19]

Lidocaine is predominantly eliminated by the liver and undergoes a large first-pass metabolism. The loading dose and infusion rate should be reduced by 50 percent in elderly patients with congestive heart failure or significant hepatic insufficiency. Central nervous system toxicity is minimized by giving the loading dose in two separate bolus injections 15 to 30 minutes apart. This allows time for the distribution of the drug and prevents the perfusion of initially high serum levels to the brain.

Anticoagulants

Elderly patients are much more sensitive to the anticoagulant effects of warfarin. This appears to be due to a reduced number of albumin binding sites, reduced activity of the hepatic mixed function oxidase system, and a reduced ability of the liver to synthesize clotting factors. The initial loading dose and maintenance doses of warfarin should be significantly reduced in older patients and monitored closely with prothrombin times. The patient should be warned about taking any other drugs concurrently without first checking with the physician. It is especially important to avoid the administration of aspirin. Acetaminophen, codeine, and ibuprofen (Motrin) can be safely administered to a patient receiving warfarin. The demonstration of occult blood in the stool or urine should not be passed off as a drug side effect but should be investigated thoroughly.[20-22]

Psychotropic Drugs

Psychotropic drugs are among the most commonly prescribed medications to elderly patients. A physician confronted with a patient with psychiatric illness should first eliminate drug induced causes (Table 5). The benzodiazepines can readily be divided into long-acting drugs (ie, chlordiazepoxide, diazepam, flurazepam) with active metabolites, and short-acting drugs (oxazepam, temazepam, lorazepam) which do not have active metabolites. The long-acting drugs are primarily metabolized by the mixed function oxidase (P-450) system. The capacity of this system to metabolize drugs has been shown to be significantly reduced in elderly patients. Therefore, when the long-acting drugs are used in an elderly patient, an excessive duration of action with drug accumulation can be expected. The short-acting drugs are not metabolized by the mixed function oxidase system and are the drugs of choice in elderly patients.[23-25]

Table 5. Iatrogenic Psychiatric Illness

Depression	Organic Brain Syndrome
Reserpine	Benzodiazepines
Propranolol	Anticholinergics
Oral contraceptives	Cimetidine (Tagamet)
Benzodiazepines	Amantadine (Symmetrel)
Methyldopa	Chlorpropamide (Diabinese)
Steroids	L-dopa
	Digitalis glycosides
	Steroids
	Tricyclic antidepressants
	Theophylline

Tricyclic antidepressants have significant anticholinergic and cardiovascular side effects. Since these drugs undergo a large first-pass metabolism in the liver, dosage reductions are generally indicated in elderly patients. A 25-mg test dose is often recommended. Orthostatic hypotension is a common side effect, and orthostatic changes in blood pressure should be measured. Orthostatic hypotension can be dangerous in older patients with left ventricular dysfunction, aortic stenosis, or compromised vascular beds. The other major cardiovascular side effect is prolongation of conduction time. These drugs should be used very cautiously in patients with pre-existing conduction defects. Doxepin (Sinequan) does not prolong conduction time in the His-Purkinje system and is the drug of choice in patients with conduction abnormalities.[26] Anticholinergic side effects can be dangerous in patients with congestive heart failure, angina pectoris, and prostatic hypertrophy. Desipramine (Norpramin) has the least anticholinergic side effects of the currently available tricyclic antide-

pressants. The sedation potential of the tricyclics should also be considered. Amitriptyline and doxepin are the most sedating, and a major portion of the dose should be given at bedtime. Protriptyline (Vivactil) has a stimulant effect, and the major portion of the dose should be given in the morning.[27]

The major side effects of the phenothiazine tranquilizers and related drugs are manifested in the cardiovascular and neurological systems. The most common cardiovascular side effect is orthostatic hypotension and is most common with the high-dose drugs (ie, chlorpromazine and thioridazine). The high-dose drugs are also more sedating but have a lower incidence of extrapyramidal reactions. Thioridazine (Mellaril) appears to have the lowest incidence of extrapyramidal side effects. The potent low-dose drugs (ie, perphenazine, thiothixene, and haloperidol) are less sedating and have a lower incidence of cardiovascular side effects. However, these drugs are more commonly associated with extrapyramidal side effects. The low-dose drugs are generally preferred in elderly patients with organic brain syndrome or significant cardiovascular disease. Antiparkinsonian drugs should not be started routinely in all patients. Should an extrapyramidal side effect develop, the antiparkinsonian drugs should be started but should not be continued indefinitely. Elderly patients who are unable to tolerate the anticholinergic side effects of some antiparkinsonian drugs may be tried on amantadine (Symmetrel). Tardive dyskinesia is a serious neurologic consequence of prolonged psychotropic drug usage. There is currently no effective treatment for tardive dyskinesia. To prevent this complication, antipsychotic drugs should be prescribed in the lowest effective dose for the shortest period of time.

Analgesics and Nonsteroidal Anti-inflammatory Drugs

Since parenteral narcotics such as meperidine and morphine sulfate undergo large first-pass metabolism in the liver, the dose of these drugs should be significantly reduced in elderly patients. In a 75-year-old patient, 50 mg of meperidine may produce the same analgesic effect as 100 mg of the drug in a younger patient.[28]

Chronic pain syndromes are much more common in older patients and are frequently caused by degenerative joint disease and other chronic illnesses; therefore, it is not surprising that elderly patients consume large quantities of analgesic drugs. Most analgesic drugs have ulcerogenic potential and create a risk of gastrointestinal hemorrhage. Because of decreased gastric emptying time, elderly patients may be more at risk for these side effects.

Aspirin has the most pronounced effect on platelet function, and small doses will irreversibly impair platelet aggregation. When aspirin is prescribed as an antiplatelet drug, efficacy may be best at very low doses (325 mg/day). Such low doses tend to preferentially affect the formation of thromboxane (A-2) without adversely affecting the function of the antithrombotic prostaglandin, prostacyclin. Although enteric-coated aspirin tablets (Ecotrin) are associated with a lower incidence of gastrointestinal hemorrhage, bioavailability may be reduced. Phenacetin is not generally recommended for chronic therapy because of the associated risk of chronic renal failure secondary to papillary necrosis and interstitial nephritis.

Many nonsteroidal anti-inflammatory drugs have been marketed during recent years. Many of these drugs have equal efficacy to aspirin but a much lower incidence of gastrointestinal toxicity. All of these drugs inhibit prostaglandin biosynthesis and affect platelet function. Ibuprofen (Motrin) and sulindac (Clinoril) appear to have a relatively low incidence of gastrointestinal toxicity and a minimal effect on bleeding time. The fenamate derivatives, such as mefanamic acid (Ponstel) or meclofenamate (Meclomen), are no more efficacious than the other agents and have a clearly higher incidence of adverse effects. All elderly patients receiving nonsteroidal anti-inflammatory drugs on a chronic basis should have periodic blood counts and stool specimens examined for occult blood.[29]

Antimicrobials

The use of aminoglycoside antibiotics in elderly patients is associated with an increased risk of nephrotoxicity and ototoxicity. These drugs are excreted entirely by the kidneys, and creatinine clearance is usually overestimated in older patients. Creatinine clearance should be carefully measured in patients receiving aminoglycoside antibiotics, and the initial dose should be chosen on the basis of creatinine clearance and body weight. Renal function should be followed during

therapy by the repeated measurement of serum creatinine. Dosage adjustments are best made on the basis of serum drug levels. Generally, both peak and trough serum drug levels are obtained. The risk of nephrotoxicity seems to correlate best with elevated trough levels.

Several antibiotics have well-known adverse effects that may be particularly dangerous in the older patient. Tetracyclines can cause a negative nitrogen balance and azotemia. Demeclocycline (Declomycin) is especially toxic to the renal tubules and can cause nephrogenic diabetes insipidus. The incidence of photosensitivity is also high with demeclocycline. Minocycline (Minocin) causes a disturbingly high incidence of vestibular reactions, which may precipitate falls or other accidents. Nitrofurantoin (Macrodantin) can cause pulmonary fibrosis, which can present as a persistent cough. The pseudomembranous colitis caused by clindamycin (Cleocin) can be associated with increased morbidity in elderly patients. Finally, the risk of isoniazid-induced hepatitis increases with age.

Topical Drugs

The absorption of potent fluorinated corticosteroids through the thin atrophic skin of elderly patients is increased. Adrenal suppression is unlikely unless large quantities of a potent preparation are applied over a large surface area on a long-term basis. Occlusive dressings also significantly increase systemic absorption.

Dry pruritic skin is a common problem in elderly patients. The urea containing creams and lotions are the most effective moisturizing preparations (ie, Aquacare, Carmol). Although not quite as effective, Eucerin cream is helpful in many patients and less expensive than the urea containing creams. Schamberg's Lotion is a useful cooling and antipruritic lotion containing 0.5 gm of methol, 1 gm of phenol, 20 gm of zinc oxide, 40 ml of calcium hydroxide solution, and peanut oil in sufficient quantity to make 100 ml.

Gastrointestinal Drugs

The sodium content of liquid antacid preparations is an important consideration in elderly patients with hypertension and congestive heart failure. Riopan contains 0.3 mg/5 cc of sodium, which is the lowest sodium content commercially available. The widely promoted product, Alka-Seltzer, is not a good choice in elderly patients. In addition to containing 276 mg of sodium per tablet, this product can cause systemic alkalosis with continued use.

Cimetidine (Tagamet) has been reported to cause mental confusion, slurred speech, delirium, and hallucinations in some elderly patients. These mental symptoms are usually rapidly reversible after the drug is discontinued. Cimetidine is a potent inhibitor of the mixed function oxidase system (P-450) and can prolong the half-life of many drugs (ie, diazepam, chlordiazepoxide, warfarin). Since cimetidine is primarily excreted unchanged in the urine, dosage reductions are appropriate when creatinine clearance is reduced.[30]

Constipation is a common problem in elderly patients. Irritant laxative preparations (ie, cascara sagrada, senna, castor oil, phenolphthalein) should be avoided since they cause laxative dependency. Initial recommendations should be directed at dietary manipulation and increased exercise. When a laxative is indicated, bulk laxatives (Metamucil, Mitrolan) are the most physiologic and generally recommended first. When bulk laxatives fail, a mild osmotic laxative such as magnesium hydroxide or lactulose (Chronulac) should be prescribed. Enemas can be prescribed as needed.

Hypoglycemics

The only orally available hypoglycemic agents are the sulfonylureas. These drugs are sometimes prescribed to treat mild type II diabetes mellitus in older patients. Tolazamide (Tolinase) is a useful preparation in older patients, since it is primarily eliminated by the liver. Chlorpropamide (Diabinese) is a long acting sulfonylurea that is primarily eliminated by the kidney. The half-life of this drug in a patient with normal renal function is 36 hours. Drug accumulation with resulting hypoglycemia is a possible side effect in elderly patients with renal insufficiency. Chlorpropamide has also been implicated in causing the syndrome of inappropriate antidiuretic hormone. The resulting hyponatremia can cause confusion, disorientation, and other signs of central nervous system dysfunction in elderly patients.[31]

Thyroid Replacement

Thyroid replacement in elderly patients should be undertaken cautiously. L-thyroxine is the drug of choice and is usually started in a dose of 0.025

mg daily. This dose is usually increased by 0.025 mg every three weeks until a maintenance dose of approximately 0.1 mg daily is obtained. The patient should be monitored closely for signs of cardiovascular toxicity and other adverse reactions. The adequacy of the replacement dose is best determined by measuring the serum thyrotropin (TSH) level. When the thyrotropin has dropped to the normal range, it can be assumed that the replacement dose is adequate.

Monitoring Drug Therapy

Every physician who sees elderly patients should thoroughly review the medication record and reassess the need of each medication. Unnecessary medication should be discontinued. It has been estimated that millions of dollars could be saved by thoroughly reviewing the medication records of nursing home patients and by discontinuing unnecessary or redundant medications. Likewise, a physician seeing an elderly patient for a particular symptom should first exclude an adverse drug effect as a cause of that symptom. There are few "real" cures in medicine, but drug induced iatrogenic illness is usually reversible and often preventable.

Indications for drugs should be considered carefully in elderly patients. When a drug is chosen, the dose should be based on the patient's hepatic or renal function and pharmacokinetic data. The patient should be monitored closely for adverse drug effects. These are often detected by history, physical examination, or laboratory data, including serum drug levels.

Medications should be discussed thoroughly with the patient and family. It is important that they have a thorough understanding of why the drug was prescribed, the consequences of not taking the drug, and common adverse drug effects. It is often helpful to indicate on the prescription label the symptom or disease for which the drug was prescribed. When a patient is taking more than one medication, a "pill wallet" or a medication chart is helpful in improving patient compliance and reducing medication errors. Medication lists should be examined closely for common drug interactions.

Prescription medications are a double-edged sword. Although they can produce a gratifying response, they may also produce serious adverse effect. A conscientious physician who chooses a drug and dosage wisely and monitors the patient closely for adverse effects will maximize the probability of therapeutic success.

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