

**Health Promotion and Aging**  
**"MEDICATIONS AND GERIATRICS"**

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**I. Introduction and General Overview**

Health promotion and disease prevention in the elderly is both appealing and worthy of our attention. While old age is not preventable, much of the disease and disability which is common in late life is preventable.<sup>1</sup> The rational use of medications, at both the policy and clinical level, has an important place in achieving this end, providing an important component in a health promotion strategy for healthy aging. Rowe and Kahn have cautioned against a "gerontology of the usual."<sup>2</sup> The focus on typical aging as "normal" ignores the enormous heterogeneity in this population. This may mislead scientists and policy makers to view what is "usual" as a reasonable health objective for older Americans.

**II. Basic Demographics and Population Data**

In 1987, about 12% of the U.S. population is 65-years or older. By 1990, the 65 and older group will reach 12.7% of the population; by 2000 the percentage rises to 13.1; and by 2020, to 17.3%. By the year 2020, the 65 and over population will have increased by 102%, compared to the 31% growth for the entire U.S. population for the same 40 year period.<sup>3</sup>

Changes will also be taking place within the elderly population itself. Not only will there be more citizens over 65 years of age, both in absolute number and percentage, but individuals within this age group will be living longer and, on the average, may tend to be more frail, and possibly in greater need of medical care. The older age groups, especially those over 75, will increase most dramatically. The current number of persons over 85 (2.7 million) will double by the end of the century. Conservative estimates to the year 2050 indicate that at least 50% of Americans will survive to their 85th birthday, with the 85 years and older population constituting at least 15 million people.<sup>4</sup>

**III. Health Characteristics**

Three general health characteristics of older U.S. residents are relevant to medications and geriatrics. First, the pattern of health service utilization influences the opportunities for receiving a prescription; second, the epidemiology of disease (especially chronic disease) influences the duration of treatment; and third, drug activity in the aging body influences therapeutic safety and efficacy.

**A. Utilization of Health Services.** Prescription drugs are prescribed for the elderly primarily as outpatients making physician office visits, as inpatients in long-term care facilities, and as hospitalized patients, as well as upon discharge from health care institutions. Persons 65 and older account for 20.5% of physician office visits in 1985.<sup>5</sup> And while most elderly are not in nursing homes, they did occupy 88% of the available nursing home beds in 1985.<sup>6</sup> And in 1986 persons 65 and older accounted for more than 40% of the hospitalizations in this country, staying an average 8.5 days compared to 6.8 days for 45-64 years of age.<sup>7</sup> "In the near future, the majority of all users of health and health related services with the exception of obstetrics and pediatrics will be persons over 65."<sup>8</sup>

**B. The Epidemiology of Disease.** As briefly discussed above, the elderly in America are more likely to use health services than are younger age groups.<sup>8</sup> This is explained in part by the fact that in spite of fewer acute illnesses, their recovery time is often longer; the fact that they are nearly twice as likely to suffer from a chronic illness; and the possibility that they may overuse services relative to true need.<sup>9,10</sup> In view of this reality the health care system's response requires strategies that are often quite different than those for younger persons because of the following:

*the prevalence of chronic disease.* Eighty percent of persons 65 years and older have one or more chronic diseases. Certain of these diseases are largely age dependent, such as coronary artery disease and dementia of the Alzheimer's type; other diseases, such as most cancers, are considered age related.<sup>11</sup>

*multiple pathology.* The existence of several simultaneously active conditions is much more prevalent in the aged than in those younger.

*nonspecific presentation of disease.* Several diseases which occur at all ages have a different natural history in the elderly. Almost any of the classic signs or symptoms of disease are present in the elderly in uncharacteristic ways. Instead of usually anticipated presentations, diseases often give rise to nonspecific problems which may be incorrectly identified as due to aging rather than due to disease. These nonspecific problems include falling, dizziness, acute confusion, new incontinence, weight loss, failure to thrive, etc.

*silent presentation of disease.* Especially likely to be obscured in the elderly are pulmonary embolism, pneumonia, cancer, acute surgical abdomen, thyrotoxicosis, depression, drug intoxication, myxedema, myocardial infarction, alcoholism.<sup>12,13</sup>

**C. Pharmacokinetics and Pharmacodynamics of Drugs.** Drug disposition in the body of an elderly patient may be quite different than in a similar patient forty years younger. Although these changes may not necessarily occur, when present they are largely the result of age related changes in body composition, renal and hepatic function, and concurrent disease states. In addition, an older patient may not respond to a given drug concentration in the same manner as a younger individual.<sup>14,15</sup> Age related physiologic changes in older patients dictate that while the standard guidelines for applying pharmacokinetic principles often apply, they must be approached with caution because some of the usual assumptions may not be valid. In particular, the clinician must more carefully consider possible changes in body composition and vital organ function.

**ABSORPTION /** A number of aging-related physiologic changes occur in the gastrointestinal tract (GI) which increase the possibility of altered drug absorption. With advancing age intestinal blood flow may decrease; muscle tone and motor activity in the GI tract may decline; and mucosal cells may have atrophied, reducing both gastric secretory and absorptive function. The elderly demonstrate prolonged and widely variable gastric emptying times when compared to younger groups.<sup>16</sup> In addition, the pH of GI fluid is increased in the elderly, a change that may effect the absorption of calcium.<sup>17</sup> In spite of these demonstrated and theoretical GI changes, altered absorption does not appear to be a clinically important factor in dosage calculations for older patients.<sup>18</sup>

**DISTRIBUTION /** Body composition undergoes noteworthy changes over a lifetime of 70+ years. Body fat increases, muscle mass decreases, and total body water decreases. By age 70 greater than 30 percent of body weight in a given individual may be fat. On the other hand, muscle mass contributes a smaller proportion of body weight, declining by an estimated 25 to 30 percent by age 70. Total body water decreases in the elderly from 13 to 18 percent.<sup>19,20</sup> These changes can have a clinically significant impact on the distribution of both water soluble and lipid soluble drugs. As a rule, with substantially increased age, water soluble drugs will have decreased distribution, while lipid soluble medication will have increased distribution.

The plasma protein binding of drugs in the elderly may be altered.<sup>21</sup> The two major plasma proteins are albumin and alpha-1-acid glycoprotein. Older patients often have a lower than normal serum albumin level, usually the result of decreased albumin production. Also, an

increased level of alpha-1-acid glycoprotein has been associated with advanced age.<sup>21</sup> The potential significance of these changes are either an increased free fraction of drugs bound to albumin (e.g. warfarin, phenytoin) or decreased free fraction of drugs bound to alpha-1-acid glycoprotein (e.g. lidocaine, propranolol). These alterations in binding may lead to the erroneous clinical judgments based on misinterpretation of serum blood levels.

**METABOLISM** / Phase I oxidative metabolism can be impaired in the elderly patient due to decreased microsomal enzyme activity. Also, the metabolism of drugs with high hepatic extraction ratios can be impaired due to a decrease in hepatic blood flow.<sup>22</sup> This is particularly important when prescribing certain drugs such as diazepam, quinidine, theophylline, propranolol, and imipramine. Easily estimating the extent of impaired metabolic function is not currently possible; consequently, dosage adjustments necessitated by metabolic impairment are, at best, estimates based on investigational and clinical experience.

Hepatic Phase II metabolism via conjugation is not meaningfully altered with advancing age. Consequently age related changes in clearance of drugs metabolized by glucuronidation clearance have not been reported. For example, oxazepam, lorazepam, and temazepam doses need not be reduced in older patients on the basis of hepatic function alone.

**ELIMINATION** / Glomerular filtration rate (GFR) declines steadily with increasing age. Because of the typical decline of muscle mass with advancing age, production of creatinine also declines. This produces serum creatinine levels usually considered normal for younger persons, but unreliable as an indicator of renal function in the older person. Thus, a calculated creatinine clearance is recommended when considering the proper dose of such drugs as digoxin, cimetidine, many antibiotics, and active metabolites such as N-acetylprocainamide and normeperidine.<sup>23,24</sup>

**PHARMACODYNAMICS** / The term pharmacodynamics usually refers to the magnitude of pharmacological effect that results from the interaction of drugs with receptors at the site of action. There is little information about the pharmacodynamics of drugs in the elderly, but an increased "sensitivity" to a number of drugs has been reported.<sup>20,25</sup> Perhaps the most widely reported is the enhanced pharmacological effect of narcotic analgesics in the elderly.<sup>26,27</sup> In a study by Kaiko it was found that elderly cancer patients, who received intramuscular morphine post-operatively, had significantly greater total pain relief and duration of pain relief than their younger counterparts. No information regarding adverse effects was reported.<sup>28</sup> This study confirmed similar findings reported in an earlier study by Bellville, et al.<sup>29</sup> Demonstrating decreased pharmacodynamic sensitivity, Vestal et al. have reported a reduction in response to both beta adrenergic agonist and antagonist drugs in the elderly.<sup>30</sup> From these and similar reports there is some evidence that age-related pharmacodynamic changes can occur. For the most part whether these alterations are due to diminished homeostatic mechanisms, chronic disease, or changes at the receptor or post-receptor remains to be determined.<sup>20,25</sup>

#### **IV. Areas of Particular Interest**

Medications are usually beneficial, sometimes of no value, and on rare occasion detrimental in their contribution to the health of the elderly. Numerous areas are of particular interest with regard to drugs for older patients. The few areas discussed in this background paper are the extent and pattern of drug use among older patients; the health promoting benefits the elderly derive from medications; their susceptibility to untoward effects of drugs; the potential for new technologies to benefit the elderly; successful interventions and programs; and selected deficiencies in current programs and services.

**A. The Extent of Drug Use.** The elderly take prescription and non-prescription drugs to a greater extent than younger persons. This appears to be so because their greater use of health services makes them more likely to receive prescriptions or make self-medication decisions.

**PRESCRIPTION DRUG USE** / As previously mentioned, the elderly make up 12% of the U.S. population. It is estimated however that this group accounts for approximately 30% of all drugs prescribed in the U.S.<sup>5,31</sup> In 1982 all consumers spent \$14.5 billion for prescriptions dispensed by community pharmacies.<sup>32</sup> The elderly's precise proportion of that cost is not known, but if it was 30% that would be \$4.35 billion. An FDA study found that those over 75 years of age

received the most prescriptions in 1982, averaging almost 17 annually. The "young-old," those 65 to 74, received only 13.6 that year. These numbers are much larger than the averages of those in the 55 to 64 age group (9.3 prescriptions) and the 45 to 54 age group (6.9 prescriptions).<sup>33</sup>

The 1985 National Ambulatory Medical Care Survey of office based physicians found that elderly women accounted for 12.5 percent of all visits and 17.7 percent of visits in which drugs were prescribed; elderly men accounted for 8.0 percent of visits and nearly 11 percent of visits involving drug prescription.<sup>32</sup> Overall at least one drug was prescribed or provided in over 68 percent of office visits by those 65 years of age and older.

**OTC DRUG USE / Self medication** as part of self-care seems to be one of the most important and frequent health maintenance actions taken by the elderly. A recent study of rural elderly found 65% of those surveyed to have used over the counter (OTC) medications in the previous two weeks, with women taking more than men.<sup>34</sup> This was consistent with findings from an earlier study of an elderly population in which 64% had taken OTC medications; again, women used more than men.<sup>35</sup> Respondents in this study reported consuming in a one day period an average of 1.74 prescription drugs and 1.13 over-the-counter drugs.<sup>34</sup>

**B. Patterns of Drug Use.** Drug use patterns in the elderly vary according to the populations in which data is collected. The best defined data comes from ambulatory elderly populations. Two ongoing programs, the Dunedin Program in Florida and the N.I.A.'s Established Populations for Epidemiologic Studies of the Elderly (EPESE), provide the most extensive and detailed information about both prescribed and OTC medications in a controlled study population or cohort. The Dunedin Program which has screened approximately 3,000 elderly each year since 1978 for undetected medical disorders, has also collected patient-recorded information about prescribed and OTC medication. Over a five-year period 93% of patients in that population took some medication, with a mean of 3.7 medications at the time of interview. The study also found women to be consuming more than men, and drug use increasing with advancing age.<sup>36</sup> The most common therapeutic indications for all drugs were antihypertensives, non-narcotic analgesics, antirheumatics, various vitamins and cathartics. Striking changes over the five year period include an increase in mean drug use (from 3.2 medications) and a considerable increase in nutritional supplement use.<sup>35</sup>

The EPESE project, a community-based surveillance program funded by the National Institute of Aging, is being conducted at four research sites; New Haven (Yale University), East Boston (Harvard University), rural Iowa (University of Iowa), and the Piedmont area of North Carolina (Duke University). Extensive information regarding both prescription and OTC medication use is being collected as part of these in-home surveys of between 3,000 to 4,500 community elderly. The first published report of medication use in an EPESE population was from Iowa where 88% of patients took some medication, with the mean being 2.87 drugs. In this population medication use increased with age and was greater in women.<sup>34</sup> The most common therapeutic indications for drugs were cardiovascular, analgesics, vitamins and nutritional supplements, gastrointestinal products and CNS agents. Analgesics, vitamins, and GI agents (e.g., laxatives) were the most frequently taken over-the-counter therapeutic categories in Iowa among rural elderly.<sup>34</sup> In fact, products classified as "analgesics and antipyretics" constituted over 39% of the reported OTC drug use; and three most frequently mentioned categories accounted for more than 94.1% of this use. While the Dunedin and Iowa populations and methods are not comparable, the most distinguishing difference is the apparently greater use of drugs seen in the Florida population.

Additional information about commonly prescribed medications for ambulatory elderly comes from a variety of sources. The most recent information (1986) is from two electronic data bases: IMS America Ltd. (Ambler, PA), and Pharmaceutical Data Services [PDS] (Scottsdale, AZ).<sup>37,38</sup> The top five therapeutic classes prescribed for the elderly according to the IMS data were digitalis preparations, diuretics, beta-blockers, nitrates, and antiarthritics. The PDS data, reflecting prescription drugs dispensed, showed the top five drugs for the elderly to be hydrochlorothiazide and triamterene, digoxin, potassium chloride, nitroglycerin, and furosemide.

Drug use patterns from institutional settings are less well defined. A 1976 survey of long-term care facilities found that most patients received between 4 and 7 medications with the mean being 6.1 drugs.<sup>39</sup> The most common therapeutic indications were cathartics, analgesics,

tranquilizers, sedative/hypnotics, and vitamins. According to PDS, the top five drug products dispensed to elderly nursing home residents in 1986 were digoxin, furosemide, potassium chloride, dipyridamole, and nitroglycerin.<sup>38</sup> This pattern reasonably reflected the frequency of use these products had among non-institutionalized elderly that year. In alarming contrast, the sixth and seventh ranking drugs among elderly nursing home residents were haloperidol and thioridazine HCl; among non-institutionalized elderly these same agents ranked 99th and 90th respectively.<sup>38</sup> This report also revealed that during the first quarter of 1986, 59.2% of the elderly in the nursing homes received 4 or more prescriptions, compared to 35% of the non-institutionalized elderly.

Drug usage in hospitalized elderly is available from a variety of sources. A drug use surveillance project on a geriatric specialty unit found 500 of 521 patients to be given medications. Patients observed during the study period were given an average of 6.1 medications. In order, the most frequently used drugs were diuretics, antibiotics, bronchodilators, and analgesics.<sup>40</sup> Another study of 56 hospitalized elderly patients reported the mean drug use to be 4.1 medications prescribed for chronic use with the most common therapeutic indications being cathartics, analgesics, vitamins, diuretics, and cardiac drugs.<sup>41</sup>

**C. Health Promotion Benefits of Drug Therapy.** Health promotion strategies, particularly in older populations, must clearly rely on both social-behavioral and medical strategies. Many maladies of old age can be traced to health risk behaviors of young adulthood, and as a result prevention is often viewed as having little value as a health strategy after 65 years of age. Kannel and Gordon have suggested "that because of the relatively high incidence of mortality in the elderly the absolute impact of preventive measures short-term may actually be greater in the elderly than the younger despite a lesser relative impact."<sup>42</sup>

Since that suggestion, made in 1977, the preventive value of treating diastolic-systolic hypertension in the elderly has been demonstrated. The V.A. cooperative study demonstrated a 54 percent reduction in fatal and nonfatal cardiovascular events in the 60 years and over age group.<sup>43</sup> The Hypertension Detection and Follow-up Program found that older patients receiving drug therapy according to structured guidelines (otherwise termed "stepped-care") had lower incidence of stroke and lower mortality than age matched controls referred to their usual "regular care" for management.<sup>44</sup> And, results from the European Working Party on High Blood Pressure in the Elderly Trial have shown dramatic reductions in morbidity and mortality among drug treatment subjects over a seven year period.<sup>45</sup> Of course the importance of attentive monitoring during treatment cannot be over emphasized; anti-hypertensive medications are among the most widely implicated contributors to adverse drug reactions in the elderly [reviewed later in this paper].

The efficacy of influenza vaccine was evaluated in nursing homes of Genesee County, Michigan, during the winter of 1982-83. Investigators found the use of influenza vaccine to reduce both incidence and severity of influenza virus infections among the elderly.<sup>46</sup> A positive cost-effectiveness analysis of influenza vaccination programs for the elderly was reported comparing medical costs and health effects between vaccinated and unvaccinated elderly from 1971-1972 through 1977-1978.<sup>47</sup> Despite belief in the preventive value of the vaccine, medical compliance with recommendations for its use has been poor; institutional policy appears to be the best means for accomplishing wide spread immunization.<sup>48</sup>

Disability and immobility are associated with fractures in older persons; and fractures are associated with low bone mass.<sup>49</sup> The N.I.H. estimates that about 1.3 million fractures a year can be attributed to osteoporosis in people aged 45 years and older.<sup>50</sup> As one of the most prevalent afflictions of advancing age, osteoporosis-related vertebral fractures burden one-third of women by age 65. By age 81 hip fractures, usually associated with osteoporosis, will have stricken one-third of the women.<sup>51</sup> An effective means of preventing the loss of bone mass in postmenopausal women is regular use of estrogen therapy, particularly when combined with calcium supplements.<sup>52,53,54</sup> The FDA recently acknowledged this preventive indication to be an effective use of estrogens when taken for 21 or every 28 days and combined with calcium supplements and exercise.

A variety of useful but less well documented preventive and protective actions of drugs have been reported. For example, a case-control study of 300 cataract patients and 609 controls found a protective effect from long-term use of aspirin-like analgesics.<sup>56</sup> Such findings clearly require methodologic scrutiny and additional investigation. But they also ought to encourage the continuing search for agents with potential for preventive/protective impact on common disabling conditions of advanced years.

**D. Health Risks and Problems Associated With Medications.** The major areas of concern with regard to health risks and problems associated with geriatric drug therapy can be organized as bio-medical, behavioral, economic, and health policy/health services. Conversely, these areas also represent important targets for drug oriented health promotion interventions. In general, issues reviewed independently in this background paper (e.g. adverse drug reactions, compliance, costs, access, and attitudes) are very much interdependent, and an integrated approach to solutions is recommended.

**DRUG RELATED BIO-MEDICAL ISSUES /** Aging is associated with a variety of physical changes and health problems. Adverse drug reactions also present in a wide variety of symptoms throughout the body. A major challenge for the clinician is to distinguish between symptoms of aging and those associated with drug therapy. Mental disturbances, fatigue, depression, and syncope are examples of complaints that are associated with commonly encountered conditions as well as frequently prescribed medications.<sup>56</sup>

**1. THE EPIDEMIOLOGY OF ADRs.** Just as drug use patterns vary with populations, incidence and prevalence data for adverse drug reactions (ADRs) is quite dependent on data collection methods and settings in which studies have been conducted. Multicenter collaborative drug surveillance programs, voluntary reporting to FDA, cohort surveillance, the control phase of intervention demonstrations, institutional or population specific prevalence surveys, and computerized record linkage of secondary data sets have provided the most enlightening perspective on ADRs in the elderly thus far.

The Boston Collaborative Drug Surveillance Program (BCDSP) formalized and standardized clinical data collection on medication use and effects in a consortium of hospitals. Routine screening procedures have been used by BCDSP to correlate patient factors and drug response. From this effort dozens of adverse effects associated with drug therapy have been identified; advanced age has been an important variable in several instances (e.g. heparin in older women<sup>57</sup> and high dose flurazepam in older patients<sup>58</sup>).

The FDA has been collecting reports of suspected and known adverse drug reactions (ADR's) since 1968. The data has limitations because of the spontaneous and voluntary nature of the reporting system. Nevertheless, the value of summary information from this data set to alert researchers and clinicians to drugs worthy of more careful attention should not be overlooked. Recently FDA data from the 15 year period 1968-82 was tabulated to identify medications which may cause the older patient untoward effects.<sup>59</sup> From this analysis the five generic drug classes with the highest reported adverse drug reactions were identified. These were, in order, antiparkinsonian drugs, antibiotics, antiarthritics, antiarrhythmics and diuretics. The most recent data from FDA spontaneous reporting indicates an overall rate of 8.5 ADR reports per 100,000 population; the rate among those 65 and older is nearly double that.<sup>60</sup>

Drug induced admissions to hospital were examined along with other iatrogenic causes of hospitalization at a 769-bed urban teaching hospital.<sup>61</sup> In that institution 4.2% of admissions during two summer months were attributed to medication; half of which were considered by the investigators to be potentially avoidable. Medications accounted for 77% of all iatrogenic admissions. The average age among all iatrogenic admissions was 55 years. Another report of 293 admissions to a family medicine inpatient service found 15.4% to be drug-related with almost one-half occurring in patients 60 years of age or older.<sup>62</sup>

The occurrence of ADRs during hospital stays provides another perspective. During March and April of 1981 records for all admissions to Denver's VA Medical Center were reviewed.<sup>63</sup> In this study the occurrence of hospital associated iatrogenic complications for veterans aged 65 and older was compared with younger patients. The younger group had no complications caused by

drug reactions while 17.7 percent of the older group experienced an ADR. This rate is consistent with those reported in other studies.<sup>64,65</sup> The differences between hospitals are perhaps due to the use of different criteria for determining a drug reaction.

Growing awareness of aging has stimulated an increasing number of investigators to use large computerized data sets to focus on drugs for their possible etiologic part in common problems of old age. Two examples for illustrative purposes are included. (1) An association between psychotropic drug use and hip fractures has been identified using computerized Medicaid files; dementia as a confounding variable did not appear to influence the results.<sup>66</sup> (2) A slightly increased risk of hospitalization because of gastrointestinal bleeding has been noted among elderly users of nonsteroidal anti-inflammatory drugs compared to nonusers at the Group Health Cooperative of Puget Sound.<sup>67</sup>

**2. FACTORS CONTRIBUTING TO ADRs.** It's estimated that at least 60 percent of adverse drug reactions are an extension of normal pharmacologic action.<sup>68,69</sup> Because most adverse effects are pharmacologic and usually well-known minor reactions, many should be preventable with more careful prescribing, monitoring, and patient education.

Elderly patients are at a higher risk of developing drug reactions than the general population. Several factors are known to predispose older persons to this excess risk. The first, and perhaps strongest factor is multiple drug use. Perhaps the first approach to preventing adverse drug reactions is to limit the number of drugs. This would not only reduce the chances of side effects occurring, but also reduce the possibility of drug interactions.<sup>56</sup>

**Polypharmacy ...** The incidence of polypharmacy or multiple medication use in the elderly is substantial.<sup>34,36</sup> One of the major associated problems is adverse drug reactions.<sup>70</sup> Williamson and Chopin found an increasing prevalence of ADRs as the number of prescribed drugs increased, occurring in 10.8% of those taking one drug and 27.0% of those taking six.<sup>71</sup> Another study of ambulatory elderly with dementia also found an increased incidence at ADR's with an increased number of medications.<sup>72</sup>

A number of factors contribute to the problem of polypharmacy.<sup>73</sup> Patients who use multiple physicians and pharmacies run the risk of receiving drugs that are therapeutic duplicates and drugs that interact since the health care professionals they see may not be completely informed about other prescriptions. In addition, there is a greater risk of medication errors and/or noncompliance due to polypharmacy.<sup>74</sup>

**Pharmacokinetic and Pharmacodynamic Changes ...** As previously mentioned, there are a number of possibly age-related physiological changes that may effect the pharmacokinetics of drugs in the elderly. There is a possibility of adverse drug reactions occurring when total body clearance of drugs is reduced either due to decreased hepatic metabolism or renal excretion. This risk is increased because the higher resulting plasma concentration should correlate with higher concentrations at the receptor site with an accompanying chance of enhanced pharmacological effects. In addition, regardless of pharmacokinetic changes, the elderly may experience enhanced pharmacodynamic response to drugs.

Often, however, it is difficult to determine which mechanisms, if not both, simultaneously contribute to adverse drug reactions. For example, a study from the Boston Collaborative Group has shown that at high doses of flurazepam (= or > 30mg) 39% of patients 70 years of age or older, experienced adverse drug reactions.<sup>58</sup> This compared to an incidence of 2% in the same group taking 15mg/day of flurazepam. A later study of flurazepam kinetics found a prolongation of its half-life in elderly men.<sup>75</sup> However, there are several studies of similar benzodiazepines in which the elderly had greater central nervous system sensitivity than younger subjects despite having the same drug plasma concentrations.<sup>76,77</sup>

**Drug Interactions ...** Traditionally, the term drug interaction (DI) has been defined as the effect -- either favorable or unfavorable -- that the administration of one drug has on another drug. Only a few studies examining DI's in the elderly have been reported. In a study of 573 hospitalized elderly, 2.16% of prescriptions written during their hospitalization produced potential drug interactions.<sup>78</sup> The investigators classified 78.2% of those interactions as avoidable or probably avoidable. Drug interactions in a 1975 nursing home survey of 562 patients were found in 5.8% of medication orders.<sup>79</sup> Another study of 132 nursing homes and 11,173 patients found

that 2.7% of patients had clinically significant drug interactions occurring.<sup>80</sup> The occurrence of drug interactions among 1,094 ambulatory elderly was found to be much greater than that in the institutional populations (15%).<sup>81</sup>

It is not clear what proportion of potential drug-drug interactions are actually of clinical significance. For example, in one study 80% of the patients only required close patient monitoring as opposed to dosage reduction or drug discontinuance.<sup>80</sup> Still, the elderly are at an apparently increased risk for drug interactions as a consequence of the prevalence of polypharmacy. Also, in individual elderly patients who have altered homeostatic mechanisms and limited functional reserves, drug interactions may cause significant morbidity.

There are two major types of drug-drug interactions: pharmacokinetic and pharmacodynamic. Pharmacokinetic drug interactions occur when one drug alters the absorption, distribution, metabolism, or elimination of another drug. Interactions with the greatest potential for adverse drug reactions are those involving a decrease in the total body clearance of drugs with a narrow therapeutic index. For example, cimetidine has been shown to decrease the clearance of antipyrine, a marker of oxidative liver metabolism.<sup>82</sup> Pharmacodynamic drug interactions occur when one drug either enhances or diminishes the pharmacological effect of the other drug. This usually involves an interaction at the site of action or the receptor level. Of particular importance in the elderly is the cumulative effect of drugs with different desired pharmacological effects but similar side effects. For example, alcohol is reported to significantly contribute to sedation experienced by patients taking drugs with central nervous system depression side effects such as antihypertensives or psychotropics.<sup>83</sup>

Drug interactions in an even broader context include their adverse interactions with disease processes, foods, or laboratory tests. Drug-disease interactions, although less common than drug-drug interactions, have a greater potential to produce clinically meaningful adverse effects.<sup>78,81</sup> Information about drug-food (drug-nutrient) interactions is increasing.<sup>84</sup> It is well known that some foods can alter the pharmacokinetics of drugs, but drugs can alter appetite and/or cause vitamin deficiencies as well.<sup>84</sup> An area of current research interest is the effect of nutritional deficiencies on hepatic function and drug metabolism.<sup>85</sup> Drug-lab interactions (drug induced alterations of laboratory values) require careful evaluation and interpretation. They may indicate drug-induced illness or statistically significant, but clinically insignificant changes in laboratory test values. With growing interest in self-care and the in-vitro home diagnostic market, it will be imperative that patients and health care professionals understand that drugs may interfere with test results.<sup>86</sup>

3. BIO-EQUIVALENCE AND GENERICS. Generic prescription products provide a potential cost savings for the elderly. However, this potential has not been fully realized. The older consumer has shown reluctance to request generics in spite of potential savings. Reasons include perceived safety, efficacy, and financial risks; preference for the known product; and uncertainty about quality.<sup>87,88,89</sup>

There is a considerable debate about the use of generic drugs.<sup>90</sup> Since the passage of the 1984 Drug Price Competition and Patient Term Restoration Act, there has been an increasing number of generic products approved by the FDA.<sup>91</sup> One potential benefit of generics is that they are usually less expensive than brand name drugs. This should translate to cost savings for elderly patients. A recent study, however, questioned the cost savings of generic drugs and found wide variations in the prices of generic and brand name drugs.<sup>92</sup> Some have used this data to conclude that "it is not unusual for a generic drug to cost more than a brand name drug."<sup>93</sup> It is important to point out that in this study the consumer usually paid less for generics. Also, the study was conducted during 1984 before the new law took full effect.

Concerns have also been raised about the efficacy of generic drugs in the elderly.<sup>94,95</sup> This may stem from the fact that prior to approval for marketing, the studies required to prove bioequivalence are single-dose bioavailability studies of only 20-30 young health male volunteers. In addition, statistical variations as great as a 30% difference in generic vs. brand name drugs are acceptable.<sup>90</sup> Although the question of how this information specifically relates to the elderly patient is not fully answered, it is important to note that since 1984 there has not been a documented report to the FDA of a serious problem with a generic product.<sup>96</sup>



**BEHAVIORAL ISSUES /** The elderly appear to be particularly vulnerable to their own attitudes toward taking medications and the attitudes of others providing care. Straus has reviewed the complexity of behavioral issues as a risk factor in geriatric drug use.<sup>97</sup> Issues of compliance and attitudes provide a useful background to the larger topic.

**1. COMPLIANCE.** Assuming that a certain prescribed or OTC medication is beneficial, medication compliance or adherence is imperative to achieve therapeutic success. Numerous studies have shown, however, that whenever self administration or discretionary action is involved, patients frequently fail to take their medication as prescribed.<sup>98,99,100,101</sup> Patient noncompliance to prescribed therapies can have serious consequences. First and foremost, noncompliance can neutralize any therapeutic benefits of medical care rendered. Second, medication errors and/or medication noncompliance can lead to adverse drug reactions. Third, it has been associated with higher rates of hospitalization, longer length of stay in the hospital, and increased ambulatory visits, resulting in additional and unnecessary diagnostic and treatment procedures that generate avoidable costs.<sup>102,103,104</sup>

There is considerable controversy whether the elderly are less compliant with medications than younger patients. Two studies among noninstitutionalized elderly conducted 24 years apart reported an approximately similar medication error rate (59% and 50%).<sup>74,98</sup> Also, when the elderly were compared to a younger population, compliance rates were again similar.<sup>105,106</sup> Indeed, noncompliance seems to be associated with an increasing number of drugs rather than an increasing number of years.<sup>107</sup> An added dimension compounding the problem at the clinical level is the fact that physicians tend to overestimate their patients' compliance with prescribed regimens.<sup>108</sup>

Patient factors implicated as contributors to noncompliance include behavioral, social, and personal considerations. There is difficulty attributing health related behaviors, such as compliance, to the aging process. Not only are there methodological constraints (prevalence data vs. life course incidence data), but health behavior is also related to the social circumstances and historical context of an individual's life.<sup>109</sup> Nonetheless, an individual's perception and response to illness clearly influence his/her drug-taking behavior.<sup>110</sup> Eraker et al. have proposed a model for patient behavior which combines components Becker's earlier Health Belief Model and patient preferences.<sup>111</sup> This thoughtful approach to the issues of compliance contends that the matter is one of shared responsibility between physician and patient. One premise of this model is that the physician's responsibility is inversely related to the degree of patient participation; thus, the less responsible the patient, the more so must be the physician.

Social isolation has been found to play a significant roll in noncompliance.<sup>112</sup> A large proportion of older Americans live alone, increasing their likelihood of having compliance problems. In addition, one-third of the approximately 20 million Americans classified as illiterate are 60 years of age and older,<sup>113</sup> compounding the potential risk of misunderstandings or lack of knowledge about therapy.<sup>114</sup> Other patient factors include personal impairments such as difficulties with vision or memory or learning disabilities,<sup>115,116</sup> and physical limitations imposed by arthritis or other handicaps.<sup>117</sup> There is also evidence that some nonadherence in the elderly may be intentional<sup>118</sup> and perhaps represent intelligent noncompliance.<sup>119</sup> In addition, it appears that economic issues play a role in noncompliance among older persons. A 1986 AARP telephone survey of a population (sample size not available) 45 years and older found 13% of those deciding against having prescription filled doing so because of cost.<sup>91</sup>

**2. ATTITUDES.** Provider attitudes may place the elderly, especially the poor elderly, at an increased for substandard medical care.<sup>120</sup> In spite of more prescriptions per office visit for older patients,<sup>5</sup> office practice encounter time with older patients is apparently less than with younger patients.<sup>121</sup> Perhaps this results from a perpetuation of the agism myths which Surgeon General Koop sees as self-fulfilling prophecies.<sup>122</sup> Wetle has suggested that this may partially be attributed to misapplication of population-based data.<sup>123</sup> Applying average life expectancy data in making individual management decisions deprives the patient of credit for surviving to the moment of care; the more appropriate issue is the life expectancy beyond this encounter for the individual patient.

ECONOMIC ISSUES / More than 30% of the national health care budget is spent on care for older Americans.<sup>3</sup> Nevertheless, this does not come close to covering the full expense of health needs of the elderly. Beyond this, out-of-pocket payments and third-party payors account for additional health expenses.

1. PERSONAL EXPENSES. A high rate of use and the large out-of-pocket expenditure for drugs place economic concerns on a par with safety and efficacy as important medication issues to be faced by the elderly. There are more elderly, and more of them are using more expensive drugs. Prescription prices in the U.S. rose 56% from January 1981 to June 1985; this far out-paced the Consumer Price Index which grew 23% over the same period. National telephone surveys by AARP in 1985 and 1986 found 62% of the elderly to be taking prescription drugs on a regular basis, with just less than half (45%) receiving some assistance from insurance or other health coverage. Among those without assistance the number of older patients paying more than \$40 each month increased from 24% to 34%.<sup>91</sup> The extent of poverty (12.4% in 1986) among older Americans has remained at or near current levels for several years.<sup>124</sup>

Currently, Medicare coverage for outpatient medications moving through legal hurdles and final implementation. Overall, the potential cost of drugs under Medicare depends on the number of participants, the number of units per participant, and the unit cost of medications prescribed. Each factor is rising. In 1967 less than 78% of Medicare beneficiaries were taking medications; by 1980 the proportion had grown to more than 80%. Over that same period the average number of prescriptions per beneficiary grew from 10.4 to 12.1 annually. Because prescription size (doses dispensed) has increased over that same period the growth curves cannot be compared, but the average prescription cost more than doubled going from \$4.00 in 1967 to \$8.05 in 1980; in 1984 the cost for Medicare beneficiaries was over \$10.00 per prescription.<sup>125</sup>

Although there are some state pharmaceutical assistance programs,<sup>126</sup> Medicare does not pay for outpatient drugs at this time. They will, however, reimburse for drugs administered as part of an office visit, with the notable omission of influenza vaccination. Perhaps Medicare use of health maintenance organizations in the future may change this policy.<sup>127</sup> For elderly patients that fall below a certain income level, Medicaid coverage of medications is available. In 1986 an estimated 6.6 percent of the elderly were covered by Medicaid insurance.<sup>128</sup> A recent study analyzing different Medicaid cost-saving programs found that the elderly had less access to "essential" medications [as determined by an expert panel (e.g., insulin, thiazides, furosemide, digoxin)].<sup>129</sup> The use of generic drugs may be an approach for patients and third parties to reduce medication costs.

New factors in understanding the cost of prescriptions are encountered each year. An estimated 5% of physicians are now dispensing drugs they prescribe, with nearly one-third of office-based MD's expected to do so "within a few years."<sup>130</sup> It's probably too early to appreciate the full impact of physician dispensing on drug costs for the elderly, but analysis by the Pennsylvania Department of Aging in the fourth quarter of 1986 found that elderly patients paid nearly \$2.00 more per prescription when doctors dispensed the medication. The report did not indicate whether wholesale cost or quantity dispensed had been controlled in the analysis.<sup>131</sup>

2. PAYMENT AND REIMBURSEMENT. A major activity now under legislative consideration and enactment is the reimbursement of outpatient drugs for Medicare beneficiaries. Regardless of the exact outcome of this activity by the current Congress, this area will be of major interest for health economists and government officials for years to come. Although the primary concern of Medicare beneficiaries is the substantial out-of-pocket costs associated with prescription drugs, the primary concern of government officials is the cost of such a provision.<sup>126</sup> Given the finite dollars that Congress envisions for this benefit and the demographics of this benefit as a dramatic growth area, further refinement and adjustment will almost certainly occur with the introduction of the benefit.

At the request of the Health Subcommittee of the Senate Finance Committee, the Office of Technology Assessment (OTA) has submitted an examination cost containment strategies and possible approaches appropriate to drug coverage under Medicare.<sup>126</sup> Some (but not all) of the specialized cost-containment mechanisms offered for further exploration by OTA include various forms of price setting, provider and patient incentive programs, beneficiary cost-sharing

programs, Federal grants to state pharmaceutical assistance programs, and developing a federal restrictive formulary.

Options for defining drug coverage under Medicare are limited. Comprehensive coverage, acknowledged by OTA to be the most expensive, might include all prescription drugs or all drugs prescribed for documented chronic diseases. Over-the-counter medications could be a component of this program. A limited coverage approach, on the other hand, could finance only selected therapeutic categories or targeted sub-populations (e.g., poor elderly or nursing home residents). Some options for specifying drug groups for coverage included determination of "life-sustaining" drugs by medical consensus, identifying drugs likely to prevent hospitalization with its associated costs, and approval only for drugs (or drug products) for which the manufacturer can demonstrate specific evidence of efficacy and safety when used by elderly patients. A third option available under Medicare is "phased-in" implementation drug coverage. This approach could allow for administrative consideration of changes in clinical practice standards, and benefit from accumulated program experience.<sup>126</sup>

**HEALTH POLICY AND HEALTH SERVICE ISSUES /** The delivery of health services and the implementation of health policy are indicators of society's expectations for health promotion. The drug component of a larger strategy is reflected in these selected examples.

**1. MEDICAID.** Although only 6.6% of the elderly were covered by Medicaid insurance in 1986, these were by definition among the least able to afford out-of-pocket health expenses.<sup>128</sup> Efforts to reduce costs and focus benefits under Medicaid have been a dominating health policy issue at the state level for several years. An analysis of the effects of a \$1.00 copayment compared to a monthly limitation of 3 prescriptions found Medicaid's monthly savings under the two systems to be comparable.<sup>129</sup> However, the proportion of "essential" medications [see pg. E-10] obtained by recipients was greater under the copayment arrangement.

One approach has been the adoption of a generic formulary for Medicaid recipients by Alabama. Under that State's provisions, reimbursement for brand name drugs will not be made when generic equivalents are available. In another tack coverage of most anti-anxiety drugs was discontinued by Kansas; while coverage of psychotherapeutic drugs has been added by Arizona.<sup>132</sup>

Recently three states (Florida, Iowa, and North Carolina) adopted Medicaid service programs that are preventive in nature, but none of the three were directed at drugs or targeted the elderly. In 1985 Michigan adopted a therapeutic drug utilization program to identify Medicaid recipients at risk for drug induced illness.<sup>132</sup> In view of the higher rate of ADRs among the elderly, successes in this program ought to have greatest benefit for older recipients of Medicaid.

In view of the the increased general use of medications<sup>38,39,133</sup> (and psychotropic drugs in particular<sup>38</sup>), preadmission screening of applicants for nursing homes may shield some from overmedication while perhaps leading to more appropriate therapy for those admitted. Minnesota recently adopted a nursing home applicant screening program, and Massachusetts was considering the same in mid-1985.<sup>132</sup>

**2. MEDICARE.** An average 17% annual increase in Medicare expenditures between 1967 and 1983 prompted the shift to a prospective payment system based on diagnostic related groups (DRG's). This change in the reimbursement system was accompanied by increased rates of hospitalization for elderly Medicaid nursing home residents in Wisconsin.<sup>134</sup> Higher drug usage is usually associated with hospitalization; whether this occurred in this population is not known.

In spite of changes since 1983 Medicare costs continue to rise; and rising health care costs have financial impact on the elderly. In dealing with the issue the 100th Congress seems to favor an approach which will limit out-of-pocket health expenses to \$2000 annually.<sup>135</sup> Proposals to expand Part B to include outpatient prescription coverage received wider support in 1987 than in previous years. Under consideration is a requirement that participating pharmacies would consent to offer medication counseling to all eligible program participants.

Prescription drug assistance under Medicare could include policy features designed to improve overall drug therapy. The OTA background paper on options for drug coverage by the Medicare Program included several policy features that might accomplish this end.<sup>126</sup> Among the options

outlined were concepts of periodic professional review of drug regimens, limiting the number of prescriptions that can be funded, requiring a single dispensing pharmacy site, rewarding safety and toxicity studies targeted at elderly patients, and providing incentives for user-friendly packaging and labeling as well as patient education services.

3. **HEALTH MAINTENANCE ORGANIZATIONS.** Medicare recipients have been able to join an HMO since April 1985. During the two years following enactment of the legislation allowing this choice, slightly more than 900,000 (5.5%) of the eligible Medicare recipients had done so.<sup>127</sup> However, serious questions have been raised about the long term feasibility of a prepaid capitation system of providing health services for the elderly.<sup>136,137</sup> In some instances the actuarial basis for capitation payments does not reflect the population served; also, if treatments are influenced by financial self-interests the patient may suffer. In addition, a few early providers have allegedly devised enrollment campaigns which made access to enrollment sites difficult for frail or handicapped elderly. It is clearly in the interest of HMOs to promote health and prevent disease among their members; whether medications become an important facet of their strategy remains to be seen. There is some evidence that annual prescriptions per person is approximately unchanged in older subscribers but declines among younger subscribers following enrollment in prepaid health plans.<sup>138</sup>

4. **PHARMACY SERVICES.** Interest in mail-order prescription services has increased in recent years. Although its advantages and disadvantages have been debated in hearings and editorials, rigorous evaluation of the risks and benefits is lacking. Costs, counseling, error rates, convenience and access are the usual issues addressed. Proponents cite advantages that include savings due to an economy of scale, better ability to monitor therapy because of less "switching" between pharmacies, and convenience for less mobile patients.<sup>139</sup> Detractors claim higher error rates, less personal counseling,<sup>140</sup> and even higher costs. In 1985 an Arizona based study reported that a 4% savings in unit costs was offset by a 9% higher utilization by mail-order users.<sup>141</sup> It reported that changes in therapy for older users brought about more frequent ordering and increased wastage.

Labeling and packaging of prescriptions for older patients ought to take into account the possibility of visual impairments and confusion about products of similar size and color.<sup>142</sup> Many pharmacists use special services and "senior discounts" to attract the older patients. If such programs succeed in establishing client loyalty, the opportunity for regular counseling and ADR monitoring should benefit the older patient.

"Brown Bag" projects are programs in which elderly are encouraged to bring medications to a convenient location for review and counseling. Their focus is the ambulatory older population, and their purpose is to detect potential medication problems and correct those that need attention. One program has reported approximately 88% of participants need reinforcement, clarification, education, or health provider follow-up.<sup>143</sup>

5. **FRAUD.** The elderly seem to be less suspicious of medications that do not produce their promoted or expected results.<sup>144</sup> Among 172 older respondents (age 60 or older) to a 1984 survey, one-half reported purchasing a health product that did not work and just over one-half of those (53%) suspected it to be quack medicine. While appropriate cautions regarding interpretation were stated, the authors pointed out that the elderly are particularly vulnerable to fraud and the consequences of quackery because they are more likely to suffer from conditions for which many quack medications are promoted.

6. **ADVERTISING.** The claims that OTC as well as prescription drugs portray, either directly or indirectly, to the elderly are an area of continuing concern. Surveillance of the prescription drug claims relating to the elderly that are made directly to consumers or through health practitioners, will continue to share an area of high interest and surveillance by FDA.

**E. Developing Technologies.** New technologies in information management, drug products, and health service delivery bode well for improvements in drug therapy for the elderly. As computerized expert diagnostic systems become more user-friendly, the power of knowledge previously available only through years of experience should make extensive information available to all that care for elderly patients.<sup>145</sup> Public awareness of the special needs of older

citizens has served to stimulate the application of new technologies in areas which benefit the elderly.

In the future, advances in technology are expected to result in the development of new dosage forms and new drug entities that will be more convenient for older patients as well as more specific and efficacious in their pharmacologic effects.<sup>146,147</sup> A number of novel drug delivery systems are currently being developed.<sup>146</sup> For example, transdermal delivery systems can extend a drug's duration of effect, and therefore should assist in improving compliance. Biotechnology advances are also expected to result in the development of numerous new therapeutic entities.<sup>147,148</sup> A number of pharmaceutical firms are currently working to develop new drugs that might reverse cognitive losses in Alzheimer patients.<sup>149</sup>

Geriatric assessment units have been referred to as examples of "new technologies" in health services, and have grown in number and scope since 1979.<sup>150</sup> A 1985 survey of 104 units found that nearly half had begun operation during the previous two years, and two-thirds of the others increased their capacity during that time. Most (approx. 60%) are outpatient units, and 27% of those reported "improvement in drug regimens" to be either their 1st or 2nd most important effect.

**F. Successful Interventions and Programs.** Drug related problems in the elderly do not usually occur in isolation. The several successful interventions reviewed here gave emphasis to a particular outcome (e.g., compliance, polypharmacy, adverse drug reactions, cost savings), but in most instances the intervention required multidisciplinary effort and cooperation, and effected more than one area of need.

**COMPLIANCE /** The success of drug-related health promotion patient interventions depends on relevance, individualization, feedback, reinforcement, and facilitation.<sup>151</sup> Ten strategies for reducing drug errors in the elderly were reviewed by Green et al. in 1986.<sup>152</sup> These investigators found facilitation to be the most common technique, with no more than half incorporating relevancy or individualizing intervention, and even fewer using feedback or reinforcement. They concluded that interventions combining interpersonal communication methods, visual materials and memory-aids had been shown to be effective means of reducing drug errors as well as related clinical symptoms in the elderly. Several of these studies compared the effectiveness of different strategies on medication compliance and errors. MacDonald, et al., found no significant difference between medication counseling and counseling with a medication calendar. Both strategies significantly improved compliance in comparison to controls.<sup>153</sup> Color-coded weekly medication packaging significantly reduced medication errors when compared to color-coded conventionally dispensed medications, medication counseling, and no intervention.<sup>154</sup> Another study compared verbal medication counseling alone and in combination with either written information, a medication calendar, or a seven day medication package.<sup>155</sup> Attitudes, knowledge, and compliance in an elderly ambulatory population were assessed. Drug knowledge was most favorably effected by verbal instruction alone or combined with a medication calendar. In contrast, patient reported compliance was improved only by the combined intervention of verbal medication counseling and use of a seven day medication package. In general, patients felt the interventions were useful with the notable exception of the medication calendar.<sup>155</sup>

**EDUCATION FOR PRESCRIBING /** There is some evidence that physician peer education can have positive impact on prescribing in general. Studies by Ray and Schaffner have shown that the prescribing of antibiotics and diazepam improves after receiving education visits from a physician.<sup>156,157,158</sup> Also, pharmacist provided drug information can favorably impact on the prescribing of specific drugs or therapeutic classes of drugs.<sup>159,160,161</sup> Avorn found improvement in the prescribing of cerebral and peripheral vasodilators, oral cephalosporins and propoxyphene after education visits by a clinical pharmacist. The program, involving 400 physicians, resulted in a 14% reduction in utilization.<sup>159</sup> Hanlon, et al., found the prescribing of the above mentioned medications and the number of medications prescribed per patient to be lower than national prescribing data in a family medicine residency program with an active clinical pharmacy program.<sup>160</sup> Finally, a controlled study showed that global prescribing practices were favorably impacted by continuing education provided by clinical pharmacists and pharmacologists.<sup>161</sup>

**ADR REDUCTION and SAVINGS /** Interventions by clinical pharmacists as consultants in long-term care facilities (LTCF's) have been documented as being effective. One study of feedback from the LTCF clinical pharmacist consultant reduced the incidence of medication errors, the number of inappropriate or unnecessary drugs, and the incidence of adverse drug reactions, thereby reducing medication and hospitalization costs.<sup>133</sup> In a long-term study evaluating the initiation, termination, and reinstatement of a consultant clinical pharmacist, it was found that there was lower drug-use, admission, discharge, and death rates during the time the consultant was with the facility.<sup>162</sup> A recent paper examining the cost-benefit ratio of pharmacist-conducted drug-regimen review in LTCF's estimated a net savings of \$220 million nationwide.<sup>163</sup>

Another study monitored adverse reactions in 2,771 randomly chosen hospitalized patients during 1969-1976. Medications as well as indications for starting and stopping therapy were tabulated, and records for the 1969-72 period were compared with those for the 1973-76 period. An active surveillance and ADR reporting program during the second period resulted in a 61% reduction in the number of patients affected by reactions to drug therapy; with the greatest reductions in the two age bands over 70 years of age (69% and 89%).<sup>164</sup>

A novel study evaluating the pharmacist as a prescriber of drugs to previously diagnosed LTCF patients, found them to be more effective than physicians in terms of number of drugs prescribed, lower number of deaths, and increased number of patients discharged to lower levels of care.<sup>165</sup> The significance of this study may not be the role of the pharmacist as an independent mid-level practitioner but extrapolating this information to include the pharmacist as an integral part of a multidisciplinary team.

**MULTIDISCIPLINARY COOPERATION /** Nursing initiative at one teaching nursing home has targeted reduction in cathartic drug use as a priority.<sup>166</sup> In nursing homes conflicting schedules limit opportunities for personal contact and direct dialogue among professionals. Although drug regimen reviews conducted by nursing personnel in Iowa intermediate care facilities have identified a variety of problems, widely variable physician responsiveness to reports and recommendations has been reported.<sup>167</sup> In Georgia Longe et al. found that written recommendations of consultant pharmacists in skilled nursing facilities were usually effective, with 72% of drug-dosage recommendations and 80% of laboratory test recommendations being accepted.<sup>168</sup> In North Carolina an interdisciplinary team review approach to drug therapy recommendations resulted in a reduction in the number of medications at one long-term care facility.<sup>169</sup>

#### **V. Priorities and Recommended Programs to Address Areas of Concern**

**THE AGING PROCESS and DRUG DEVELOPMENT /** Basic research into the aging process and the diseases of aging is needed. Distinction between aging processes and disease processes is not possible in many instances.<sup>170</sup> Investigation into the physiology of aging will contribute to needed understanding of pharmacodynamic changes and guide drug development specifically beneficial to older patients. Health promotion and disease prevention initiatives should benefit from this basic research and, perhaps lead to the development of products that will enhance the quality of life in later years.

**DRUG TESTING /** In the past, there have been few carefully carried out geriatric clinical drug trials that investigated the pharmacokinetics and pharmacodynamics of drugs in older patient samples.<sup>171</sup> However, in recent years there has been a steady increase in information about these areas of interest.<sup>172</sup> FDA labeling guidelines were revised in 1979. These guidelines directed that prescription drug labeling feature special age group indications or precautions.<sup>173</sup> It is now common for FDA new drug applications to include analyses relating age with drug responses.<sup>174</sup> Evidently Phase III clinical trials are now less likely to have excluded subjects on the basis of advanced age. At FDA, Dr. Temple expects to have a formal drug testing proposal in place in 1987.<sup>174</sup> Although there are some disagreements about the specifics of the proposal,<sup>175</sup> a number of professional groups are encouraged by the FDA's requiring the inclusion of formal testing of new drugs in the elderly and improved labeling of such information. Once a drug testing regulation is approved, the clear need will be for more studies of currently marketed drugs (Phase IV) in older patients.

Clinical drug trials in which subjects are stratified on age and factors known to alter drug disposition are controlled. These studies are needed in order to identify agents for which pharmacokinetic changes are truly age-dependent. This approach to testing would provide elderly patients with maximum benefit at minimum risk and allow companies developing new drugs to inform prescribers of true factors effecting dose.

**POST-MARKETING DRUG SURVEILLANCE** / The field of pharmacoepidemiology, or the study of drug use and drug effects using specific epidemiological methods has emerged in recent years.<sup>176</sup> Interest in post-marketing surveillance (PMS) of drugs and their effects is evident in several sectors, including the government, the pharmaceutical industry, and third party payors.<sup>177</sup> Investigations carried out once a new product has been marketed (Phase IV studies) can include careful assessment of spontaneous reports, additional clinical trials, cohort monitoring, and case control studies.<sup>178</sup> Two primary objectives of PMS are an assessment of efficacy and toxicity under conditions of actual clinical use, and an evaluation of the relative impact on approved indications.<sup>179</sup>

There are a number of data-bases which investigators utilize to study drug use, some of which were previously mentioned in this paper. Recently, there has been great interest regarding the effects of non-steroidal antiinflammatory drug since they are so widely used in the elderly; several studies utilizing the Medicaid Drug Event (Compass) Data Project,<sup>180</sup> The Boston Collaborative Drug Surveillance Program,<sup>181</sup> The American Rheumatism Association Medical Information System (Aramis),<sup>182</sup> and the FDA data-base have been published.<sup>183</sup>

In view of the evidence that older patients are at higher risk of adverse drug reactions and may exhibit atypical response to therapy, PMS in populations 65 years of age and older seems particularly advisable. Presently there are limitations due to the inherent nature of the data-bases themselves,<sup>184</sup> and the lack of a comprehensive national system.<sup>185</sup> There are, however, encouraging signs that the field of pharmacoepidemiology will continue to emerge and play an important role in knowledge of drugs and the elderly.<sup>186,187</sup>

**LACK OF TRAINED PROFESSIONALS** / Specialized knowledge of clinically important pharmacokinetic and pharmacodynamic changes that often accompany the aging process are needed for prescribing for the elderly.<sup>188,189</sup> It has been persuasively argued that many problems associated with prescribing can be avoided,<sup>69,78</sup> and yet about half the physicians delivering care in geriatric assessment units have no special training in care of the elderly.<sup>150</sup> Specialty training programs in gerontology and geriatrics offer one approach to imparting the specialized knowledge needed to avoid such problems. Unfortunately projections of population growth, particularly in the numbers of frail "old-old", strongly support the contention that requirements for geriatric specialists over the next decade will not be met.<sup>190,191,192,193</sup> At present there are 66 geriatric medicine programs and 27 geropsychiatry programs in the U.S.<sup>192</sup> A new fellowship program to train 4-6 physicians in geriatric clinical pharmacology will begin in 1988.<sup>194</sup> At a broader and more basic level, medical schools are providing only minimal training of geriatrics.<sup>191</sup>

Federal law mandates that a pharmacist review the drug regimens of all LTCF patients. This regulation has resulted in decreased exposure to unnecessary drugs and an associated decline in the cost of drugs in nursing homes. In addition adverse drug reactions and subsequent hospitalizations have also declined.<sup>163</sup> Although this role is established, there are only three accredited pharmacy residencies in geriatrics, and ten funded geriatric pharmacy fellowships in the U.S.<sup>195,196</sup> A 1985 survey of U.S. Schools of Pharmacy found that 40 schools planned to incorporate an AACP developed text on geriatrics in their coursework.<sup>197</sup> At least 10 schools indicated plans to offer geriatrics courses not previously available. The Geriatric Education Centers (GEC) Program has also stimulated expanded training in geriatric drug therapy.<sup>198</sup>

Whether responsibility for drug therapy management of elderly patients should be a shared or independent exercised, there is agreement that neither medicine<sup>199</sup> nor pharmacy<sup>196,198,200</sup> will provide an adequate number of specialized practitioners in the near future. Interdisciplinary training programs designed to enhance cooperative relationships between physicians, pharmacists and nurse-specialists should shorten the period during which the elderly can anticipate the shortage of geriatric drug specialists.

**REIMBURSEMENT FOR SERVICES /** Among issues usually associated with Medicare reimbursement, medication for the elderly is not typically considered. However, the opportunity (or risk) to receive medications begins with access to the prescriber and so reimbursement policy that effects access will probably effect drug utilization patterns as well. The American College of Physicians has recently published a position paper on alternative payment approaches for Medicare in which it suggests that inequities in the present reimbursement system "induce physicians to provide technologic and procedural services as opposed to cognitive and interpersonal services such as history taking, preventive health care, or patient education and counseling."<sup>201</sup>

**FINANCING /** An immediate assessment of the probable financial consequences of ambulatory drug coverage under Medicare is needed. The potential impact of such coverage on prescribing, pharmacy services, and self-care practices has not been studied.<sup>126</sup>

## VI. Summary

Drug therapy represents an important approach to promoting health in the elderly. Rational and judicious use of medications can enhance the quality of life for older patients with chronic diseases. Wide variations in body composition and organ system function exist among older persons. Consequently the clinical management of individual elderly patients demands caution and an appreciation of the possible variations in drug response. Respect for these nuances in drug response are essential to rational prescribing for the elderly.

It appears that drug usage in the elderly is considerable in terms of medications taken and associated expenses. There are also patterns of medication use which, while easily understood, suggest the need for greater prescribing forethought in subsets of the 65 and older population. For instance, increased prescribing for and general use of medication among older women; an increase in the number of medications with advancing age continues into the ninth decade of life; and more medications ordered in settings where higher levels of care is provided.

Changes in pharmacokinetics and pharmacodynamics can contribute to adverse drug reactions in the elderly. Polypharmacy (a major reason for drug interactions) and non-compliance (particularly excessive dosing) can also contribute to the incidence of ADRs. It is often difficult to predict the specific cause making advisable the use of lower initial doses with careful dose escalation titrated to therapeutic response.

As new drugs designed specifically for geriatric needs are developed, as additional training programs are funded, as new technology raises health costs in general, and as the number of elderly over 75 increases, the questions of "Who pays?" and "How much?" take on even more challenging dimensions. The issues to be faced in providing affordable, safe, and effective medications for older people in the U.S. are plentiful today, but will surely be even more numerous beyond the year 2000. 1988 is not too soon to begin to address them.

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