



Recent research has shown that close to 10% of the older population have at least one potentially inappropriate prescription, placing them at risk of acute hospitalization due to overdose or harmful drug interactions. The problem of polypharmacy in the aged is growing. Primary care physicians are obliged to take responsibility for coordinating the patient's care and must be aware of various aspects of medication use such as cumulative drug exposure, chronic comorbidities, changing pharmacokinetics, and prescribing habits of consultants.

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## Possible Polypharmacy Perils Await Older Adults

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### The Problem

The other day, I was consulted on a 79-year-old lady who was supposedly ingesting 12 different medications ranging across the daylight hours in all the colors of the spectrum, exhibiting various shapes and sizes. Some were to be taken before, others after, and the remainder with meals. The total number of tablets theoretically to be consumed by this lady was 62. Individually, each of these medications could have caused adverse drug reactions (ADR) and many of them are known to interact in various ways with each other. My patient exhibited a typical "final common pathway" of the results of basic research, drug trials, pharmaceutical marketing, physician prescribing practices, and pharmacist dispensing behaviour. Unfortunately for the patient in question, the option of non-compliance was not available since her husband tried his best to help her ingest this immense pharmacological load.

This lady represents an extreme example of the kind of medication problem that older patients can face in Canada. Research in Quebec, for example, has shown that approximately 10% of the older population have at least one potentially inappropriate prescription that meets the criteria for therapeutic overlapping, a high daily dose, or a harmful drug interaction.<sup>1</sup> The same study referred to the high cost of medication errors in older adults, which were the cause of 6.5–20% of admissions to hospital of older people. They went on to cite American data that indicated that the costs of polypharmacy are substantial.

Yet, it must also be pointed out that the modern pharmaceutical armamentar-

ium is more extensive and far superior to that available 30 years ago. Beta-blockers, calcium antagonists, anti-thrombotic agents, aminoglycosides, cephalosporins, and statins, to name just a few, would have been wonder drugs in the years just preceding my medical school days, which weren't so long ago.

### Sources of the Problem

Why has there been an increase in the perils of polypharmacy? An analysis of this lady's case can elucidate and underline some of the problems physicians face in treating senior citizens. First, "Mrs. Addison" patronized three specialists but had no primary care physician. Her family would refer her to each physician. When she received a new medication from one, the others were seldom made aware of this addition.

One would have hoped that the family pharmacist could have picked up any inconsistency or repetition in her prescriptions. Yet, since both husband and Mrs. Addison's children helped fill her prescriptions, it is no wonder that two different pharmacists were utilized. If only one pharmacy had been patronized, the existence of three bottles labelled Lasix, furosemide, and apofurosemide would have gone some way towards explaining her admission serum sodium of 120.

The fact of the husband's low level of education and poor vision—and his wife's mild cognitive impairment—combined to ensure further confusion about the various bottles of medication. Even when patients understand our instructions

and try to be compliant, they must deal with difficult-to-open childproof drug containers, small labels, lack of patient information, and instruction from pharmacists.

Drug toxicity in older adults depends a great deal on the pharmacokinetics of the individual medication: namely, its absorption, distribution, metabolism, and excretion (ADME). As the human organism ages, there is a natural decline in hepatic and renal function; as a result, pharmacodynamic responses are altered. It has long been known that in population studies, kidney function declines an average of 50% between the third and eighth decade,<sup>2</sup> and the decline is predominantly disease-related. Many medications are excreted primarily by the kidneys, so if we superimpose renal disease, such as that caused by long-standing diabetes or hypertension, onto the normal age-related decline it is not difficult to see why drug toxicity is so common among in the aging population.

Related to the above issue is the lack of appropriate dosage information for older people available to physicians and insufficient therapeutic evidence. Since many clinical trials exclude older adults and almost all premarketing testing occurs in young, healthy volunteers, confusion about drug safety abounds.<sup>3</sup>

For example, in my work as a geriatric consultant both in Canada and abroad I still see many physicians who start a drug such as hydrochlorothiazide for an older hypertensive at 25mg and even move up to 50mg if no response is noted. (This occurs despite the accepted dose range of 12.5–25mg in younger adults.)

As the danger of ADR increases with age for each drug, what about the patient who takes more than one medication? Since disease in old age is often chronic and multiple, the likelihood of polypharmacy is increased. The risk of drug interactions rises with the number of drugs ingested, as well as the age of the patient. (Well-known examples include the interaction of over-the-counter products containing acetylsalicylic acid with coumadin, as well as the danger of

diuretic-induced hypokalemia in the patient with arrhythmia and/or who is taking digoxin.)

A large proportion of the very old suffer from hypertension. While judicious treatment is indeed indicated in many, antihypertensives are responsible for a significant proportion of ADRs among older patients. For many years, based on their clinical experience, British geriatricians have cautioned against treating the very old with asymptomatic hypertension. A 1986 report by the European Working Party in part corroborated this impression by indicating that for those over 80 years of age, treatment of asymptomatic hypertension may do more harm than good. For the old-old, the jury is still out.<sup>4</sup>

### Risks vs. Benefits

Parkinson's disease stands as another example of a disease where the mere diagnosis should not automatically require a physician to put pen to prescription pad. There is no doubt that levodopa and related drugs have done wonders improving the quality of life and functional status of many parkinsonian patients, but the natural history of the disease is not affected by the use of medication.

Thus, the important question for the older patient diagnosed with mild Parkinson's disease is when to start therapy. For a given level of disease severity, individuals will differ in their need for initiation of such medication. The older person who can live a reasonably normal life will not necessarily be devastated by a mild bradykinesia or a mask-like facies.

I am not suggesting that old people should be denied efficacious therapy. Rather, since for older patients the risk-benefit equation leans more heavily toward the left side of the mathematical statement, I am proposing a more thoughtful approach to the question of prescribing habits.

### Guidelines

If the patient needs the medication, prescribe it in the appropriate doses and with the usual precautions. The old axiom

"start low, go slow, and sometimes say no," while not yet proven in an RCT, is still good, solid clinical advice. The toll of iatrogenic disease will surely fall if physicians think carefully before starting a new medication in a not-so-new person.

### Patient Compliance

It is interesting to note that if one controls for factors such as cognitive status, level of education, presence of language barriers and so forth, age alone does not appear to adversely affect compliance.<sup>5</sup> In fact, some authorities believe that, given their greater respect for the medical profession, those in the older cohorts may tend to be more compliant than their younger counterparts.

That being said, noncompliance does often interfere with the administration of an appropriate prescription. One of the easiest ways to encourage compliance is to simplify the regimen. For example, many antihypertensives (such as methyldopa, clonidine, and many beta-blockers) can be taken b.i.d. or even once per day. Prescribing a q.i.d. dosage simply makes the odds of missing a dose that much higher. Cueing, that is taking a medication at times of the day when the patient always performs a particular daily ritual (i.e., shaving, tooth brushing, eating breakfast), helps to encourage compliance. For the cognitively impaired patient, one must rely on relatives, friends, or a friendly home care nurse for supervision.

In order to ensure that the patient takes what the doctor prescribes and vice versa, ask the patient to bring all medications for each visit. This useful and inexpensive technique has been termed the Plastic Bag Test.

### Length of Treatment

It is worth questioning the continued need for every medication that your patient is taking. For example, many older people taking digoxin (a potentially dangerous drug due to its narrow toxic to therapeutic range) will have had it started sometime in the distant past for an indication which may likely no longer exist, either due to the patient's status or to a change in medical thinking. In

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general, a trial of discontinuation of a medication not thought to be indicated can usually be safely attempted as long as doses are decreased slowly and the patient is monitored closely.

### Conclusion

Successful and safe drug therapy for older patients is not a pipe dream. However, it does require an essentially conservative, yet not nihilistic, approach on the part of the treating physician. The primary care doctor must monitor the situation carefully and take responsibility for coordinating the patient's care. Consultants should not change the patient's drug regimen without communicating such a modification to the patient's family doctor. One must be aware of the pharmacokinetic changes that increase the risk of ADR and try to keep the total number of medications down in order to increase compliance while at the same time reducing the chance of drug interaction.

In thinking of the problem of drug therapy in older patients, remember Matz's definition of a medication: a substance which when injected into a rat will produce a scientific report. ◆

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