“Medications and the Aging Body: an overview of adverse drug reactions”

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“The very first requirement in a hospital is that it should do the sick no harm”.
-Florence Nightingale-

We human beings have been eating certain plants, or rubbing our bodies with them, or doing much the same with various parts of other animals, insects and minerals for time immemorial. We are especially drawn to ‘bitter herbs’; clays containing minerals and antibiotic fungi, as well as insects with specific properties. It turns out that we share this habit with many other animals (surprisingly, even caterpillars!), but most notably with virtually all our Primate relatives who have also been observed by dozens of researchers to do the same kinds of things with literally hundreds of different types of plants and insects. Typically they do this when they suffer from worms, diarrhea or skin infections. Even more interestingly, virtually all of these forms of self-medication used by both our nearest and most distant animal neighbors actually appear to work. Indeed, this is a little known but very important developing area of research into new drug discovery. In effect, it is just an extension of the animal model already used by pharmaceutical manufacturers to test compounds; it is just done outside the laboratory by non-captive animals. Studies of how animals behave when they become sick have been very useful in the recent discovery of new compounds, which are active against Malaria, one the world’s biggest killers of human beings.

Well, if taking medications is not exactly a new human experience, or unique to our society (or even to human beings!) what has changed is both the vast amount of medication consumed today and the
pivotal role it plays in our lives as we age—as well as in our economy. In the post-industrial "West", we live in what some anthropologists and psychologists have described as an especially ‘pain averse’ culture which emphasizes self efficacy and promotes the notion that even our demise, like most unpleasant things, can always be delayed. It is also a society experiencing extended life expectancy which means there are more individuals with multiple degenerative illnesses alive today than at any other time in human history. Exactly how they experience pain, symptoms and medication seems to vary a great deal from one culture to the next. Degenerative illnesses are ones that are promoted as requiring ever more intervention with age, and so those who suffer them are put on ‘maintenance’ prescriptions of medications—often ‘for life’. They have also become (by far) the biggest profit makers for pharmaceutical manufacturers who have an obvious interest in selling us something for every affliction they can define and ostensibly treat over the longest possible time periods. According to Fortune 500’s most recent figures, pharmaceutical companies were the third most profitable industry in 2007. What made them profitable are mainly medications associated with aging: of their top ten two are prescribed to prevent heartburn, two to lower cholesterol, one to lower high blood pressure, one to prevent heart attacks, one is for depression, one is for asthma and the others are antipsychotic drugs (including one associated with dementia). Most of these are for illnesses that are also largely preventable or can at least be delayed or reduced in severity with changes in lifestyle that include regular exercise, better diets and the avoidance of tobacco and alcohol—which are also essentially other legal, highly addictive compounds; in other words, drugs.

It is widely estimated that at in most of the developed world at least two-thirds of seniors take one or more prescription drugs every day; a quarter take four or more. Statistically, by taking six different drugs, there is about an 80 percent chance of developing at least one harmful interaction between two or more of these drugs. We call these ‘adverse drug reactions’, ADRs for short.

How big a problem is this? In the United States, it is estimated that ADRs are the fifth most common cause of death, following heart disease, cancer, strokes and lung disease. In Australia, a country of comparable size to Canada with universal health care, it is estimated that two million people a year are harmed by their medication and that 138,000 of them required hospitalization due to an ADR. What appears to be even more disturbing, especially for seniors, is that the chance of experiencing an ADR while actually in the hospital is elevated too: at least one in seven seniors (15%) in a recent large
British study experienced an ADR while hospitalized\textsuperscript{11}. People are likely to have a new set of physicians, new medications, medications at higher dosages, and are far too likely to become the victims of a medication error when hospitalized.\textsuperscript{12}

Along with the increased numbers of medications people take causing increases in ADRs, the other things we take (like non prescription drugs, vitamin and herbal supplements and food) also affect us differently as we grow older. This is because we have much more subcutaneous fat, possesses rather less muscle and retain significantly less water in our bodies as we age. Taken together these changes to our bodies is part of what leads to increased drug toxicity and increasingly frequent medication overdoses. Digestion also changes with age and the health of some organs deteriorate faster than others. So, older adults often are more sensitive to both prescription and non-prescription drugs than younger people. This affects how medication is absorbed into the bloodstream, how it reacts in all organs (not just the targeted ones), and how quickly it is eliminated from the body. Dosage amounts, however, are almost always determined by researchers testing drugs on healthy young men—who are much larger, have much faster metabolic rates and generally healthy organ function. It is no surprise then that many drugs actually reach much higher levels than desired when they are administered to older people, who are usually much smaller, have slower metabolic rates, compromised organ functions and because of differential life expectancy, are most often women. Testing drugs on healthy young men and then giving them to sick older women may actually appear to be quite foolish—but that is the current practice because it is thought to be unethical to test drugs on older volunteers, ironically due to the potential for an ADR! Potentially pregnant women are not used (few of these would be over 65, of course), and virtually anyone who might actually be ill is avoided because of the potential for most drugs to actually worsen serious conditions in at least some individuals—this is called paradoxical reaction\textsuperscript{13}. Not surprisingly then, many older people come to view themselves as ‘guinea pigs’ (the phrase they frequently use when speaking to us in our own research) with respect to the pharmaceutical industry, which apparently has little realistic notion of how their drugs may work in older persons. I am reminded of the famous quote attributed to the French philosopher, Voltaire, “Doctors are men who prescribe medicines of which they know little, to cure diseases of which they know less, in human beings of whom they know nothing”.

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Because seniors often see specialists in addition to their own doctor, they can receive new prescription medications without having the medications they are already using properly assessed. Troublesome side effects, very dangerous interactions with long term consequences and even disastrously lethal outcomes can result. Prescription drug “side effects” and interactions between medications (this includes prescription drugs, over-the-counter drugs such as aspirin, popular herbal remedies, nutritional supplements, and even daily multi-vitamins) commonly produce symptoms that include: internal bleeding, mood changes, loss of energy, difficulty walking, dizziness, confusion and other memory problems as well as incontinence. Initially, ADR symptoms are therefore very often mistaken to be new disease symptoms rather than the result of medication interactions. If not corrected, this misinterpretation can lead to ongoing incorrect diagnoses of dementia or Alzheimer's disease, along with some other serious conditions. In turn, this can result in totally inappropriate care being prescribed—often, alas, including treatment with yet even more medications! If this should result in a stroke, for example, that outcome will simply be attributed to old age alone and the family of the patient is never likely to discover the real underlying reason for death. Sometimes, the new symptoms are also just overlooked, ignored, dismissed, diminished, or simply interpreted (stereotypically) as the complaints of “old age”. I wish to emphasize that when taking prescription drugs we all need to be especially alert for: dizziness, blurred vision, constipation, incontinence, diarrhea, and nausea, sleep changes, mood changes or rashes which appear quite quickly. And, remember: loss of sight, hearing loss, confusion, memory loss, depression and incontinence are not “normal” aspects of aging. If you suspect in any way that medications could be causing you problems, ask for a complete medication review from your physician and pharmacist—make the appointment to have them go over everything you take, prescription and non-prescription drugs alike. So, include things like antacids, Ginko, so-called ‘baby aspirin’, fish oil, vitamins etc. Also, try to consult with a physician who specializes in geriatric medicine (elder care) if you take many medications; not just with a first line health provider (GP, Chiropractor, Nurse Practitioner, Naturopath, etc.). And, always consult your pharmacist.

How preventable are ADRs? Well, one recent study suggests that the majority (62%) are probably preventable. Moreover, the great majority of ADRs stems from the same small group of medications—commonly prescribed ‘blood thinners’ (anticoagulants), pain relievers and diuretics intended to increase urine flow, especially in men with enlarged prostates. While the incidence of ADRs is highest in the elderly (especially women) living independently, it has literally become an
epidemic in nursing homes (long term care facilities), where virtually all studies show that the majority of patients experience drug reactions while in care, and that these frequently can be deadly\(^{15}\). Warfarin (coumadin) is implicated in half of the top ten serious drug interactions seen in long term care situations—it reacts with both over-the-counter and prescription pain relievers given as treatment for any kind of pain associated with commonplace illnesses of old age, like arthritis. It also reacts with many antibiotics (especially sulfa drugs) potentially resulting in stroke.

Today, governments and independent (those who are not funded by large commercial interests) researchers recognize that over-medication of the elderly has become a major medical problem. I hope I’ve made it clear that this also happens far more frequently than the general public realizes, or some in the pharmaceutical industry would like known. Understandably we all have a difficult time concluding that our medicines often make us sick and have become a leading cause of death! Many independent researchers now have actually concluded that any new health problem in an older person should be considered drug induced, until proven otherwise. In Canada, it has been estimated that:

1. Seniors consume between 20% and 40% of all prescription medicines\(^{16}\).
2. 18% to 50% of all medication used by seniors is used inappropriately\(^{17}\).
3. Between 19% and 28% of hospital admissions for patients over 50 years of age occur as a result of medication problems\(^{18}\)\(^{19}\).
4. 60% of these admissions are attributed to adverse reactions to medications and 40% to inappropriate use\(^{20}\).

Marketing by both pharmaceutical companies and alternative health care business has encouraged consumers to believe that there is a “pill for every ill”. In many cases, treatments which are at least as effective as and far less intrusive than medication could provide appropriate alternatives (walking, meditation, breathing exercises, diet changes, Yoga, seniors “aquatics”, not watching TV before sleeping, volunteer work, non-caffeinated herbal teas, even simply increasing water intake). Sleeping and anti-anxiety medication, stomach remedies and laxatives are prime examples of drugs that are often used inappropriately and for which there are usually safer and less expensive remedies, often involving simple life-style changes which can lead to a higher quality of life.
Another very large part of this problem is inappropriate prescription; ADRs are not simply a problem that patients bring upon themselves, it is one that must be met by ongoing medical education too. For example, just over a decade ago, one study found that nearly a third (30.8%) of seniors in Québec had received a benzodiazepine for more than 30 consecutive days\(^{21,22}\). (Prescribing this particular compound for a month was highly questionable, even by 1994.) The effectiveness “benzos” decreases and dependency upon them increases when they are used for more than a month. They cause serious side effects which actually mimic dementia and are known to cause memory loss. I wonder what proportion of the diagnosis of Alzheimer’s disease has actually been attributable to long term benzodiazepine prescriptions given to older women, their most likely recipients and the group most often diagnosed with Alzheimer’s disease. According to studies in Québec\(^{23}\) high risk and questionable prescribing as opposed to rational prescribing has been most common for drugs associated with many mental symptoms including anxiety, depression and dementia. Like many other drugs they also result in other dangerous effects such as drowsiness and impaired coordination which increase the risk of falls and other accidents. They all interact in serious ways with many other drugs, and especially with alcohol. They have been implicated in many ADRs.

A number of very serious questions have arisen which stem from recent studies done in the United Kingdom where a large recent (2007) ‘prospective’ study\(^{24}\) of over 18,000 hospital admissions from the general adult population of people over the age of 16 revealed that 6.5% of them were due to ADRs, mainly in seniors who remained hospitalized for about eight days, accounting for 4% of the total hospital bed capacity. The projected annual cost of such admissions to the NHS in the UK was at minimum, £466m for the patients in this one study alone—much more for the country as a whole. In 2004, the department of pharmacology and therapeutics at Liverpool University suggested ADRs accounted for 5,700 deaths a year on admission to hospital in England. But, if adverse reactions after admission were added, this suggested a total of an astonishing 10,000 deaths, while deaths from ADRs among those not ever admitted to hospital, could easily be just as many again! Moreover, this means that many of the deaths from ADRs probably resulted from errors in the hospitals themselves. To put this in perspective, 3,221 people were killed on Britain's roads in that same year (2004), but roughly six times as many people were probably killed by legally prescribed drugs, many while hospitalized. So, these figures suggest that by 2004, medications taken in the UK were quite likely killing as many as 20,000 people a year, and most of those deaths were preventable\(^{25}\). The Drugs most commonly
implicated in causing hospital admissions in the U.K. included low dose aspirin, diuretics, Warfarin, and non-steroidal anti-inflammatory drugs other than aspirin; the most common reaction was serious gastrointestinal bleeding. I have cited the UK studies here because with their National Health Service, they are in many ways more comparable to Canada than is the USA, where the situation is almost certainly worse, because according to a survey conducted for the American Society of Health System Pharmacists, they take many more drugs of all kinds than anyone else—48% of all American adults take at last one prescription drug. They are the most medicated society in the world.

In Canada we know that a substantial proportion of seniors take several prescription and non-prescription medications at one time. Most studies, however, do not take increasingly popular non-prescription drugs, supplements (protein, dietary fiber, minerals and vitamins) and alternative herbal medications into account and they should; they are a very large part of this problem and most of them actually target our aging population. They also often emphasize mega-doses; and they motivate compliance usually by promising “amazing” results and gain a certain amount of placebo-related impact from their high cost alone. Nobody likes to admit they spent a small fortune on a supplement that didn’t work. Another non-prescription drug problem stems from what are called “over-the-counter, or OTC compounds available at the local pharmacy, or “Drug Store”. A large number of OTC medications for indigestion—which is also an increasingly common experience with old age—interact with medications prescribed for heart disease. Common “cold” medications are also implicated in many ADRs affecting seniors also taking prescription medications. (I have listed these below, in an appendix for your information).

It is important to understand that avoidance of drug interactions does not necessarily mean avoiding either drugs or foods. As in much of life; timing is everything. For example, in the case of Tetracycline and dairy products, they need to be consumed at different times, not necessarily eliminated from the diet. This is especially important because dairy products are such an important source of calcium for patients with osteoporosis, including many older women. Having good information about the medications you do take and timing medications around food intake can help to avoid drug interaction problems and maintain a balanced and even enriched diet. This does impact how people experience taking their medications, however. Life centered on the timing of medications can become quite regimented and understandably, people can build up some resentment to that over time. People tell us quite a bit about that in our research—and such resentments can result in people
avoiding certain important medications in order to eat with their family, or attend an important event. Or, they may just stop taking their prescription altogether, to see what happens.

In Canada for persons aged 55 and over, the average number of prescription drugs alone per person is 2.1 per year\(^{27}\). Surveys of individuals over the age 65 have reported averages of between 3.1 to 4.5 prescription drugs per person per year\(^{28}\). As the number of different drugs and number of daily doses increases with age, the less likely it is that a person will (or even can) properly manage the burdensome regime of their medications, thus also greatly increasing their susceptibility to ADRs\(^{29}\). Taking several medications has also been found to reduce correct knowledge of all of the drugs being taken—quite simply, it becomes confusing. And some drugs are only taken to diminish the side effects of other drugs; so that just adds to the confusion around why they are taken in the first place\(^{30} 31\).

A pilot research project we have lead at the Centre on Aging (COAG) at the University of Victoria and conducted together with the Vancouver Island Health Authority (VIHA) and Vancouver Island University (VIU) together with our community partner at Oceanside Senior’s Centre in Qualicum Beach is intended to address how prevention of at least some of these problems might best be achieved. Our research group includes specialties in medical anthropology, nursing, and geriatric medicine has conducted in depth interviews with seniors to find out from them how they actually experience medications in their daily lives. We think gathering this information is essential before actually trying to create a health promotion project to help avoid ADRs without compromising peoples’ health. I’ll just list some preliminary findings here.\(^{32}\)

I should begin by noting that while most of the people our research team spoke with felt quite uneasy about the amount of medication they were taking, and wished to take less, if possible, they also did not appear to know very much about the most common kinds of drug interactions they or others might experience. Generally, the people with whom we spoke seem never to have been offered this advice, or were not offered it in an effective way. Written information, other than that which came with their prescription, was generally missing and it remains for most of the people we interviewed, something in the realm of expert knowledge. Any health promotion project which we might create to try to deal with the problem of ADRs will have to: a) help people to learn more about them and 2) convince health professionals to more effectively share information about them with their patients as well. This means ‘de-mystifying’ part of the core of medical practice today; one where much physician power
resides—what we might describe as the ‘prescription’ ritual. This is where indecipherable code is sent on a tiny slip of paper via a patient from a doctor to a pharmacist who then decodes it, and dispenses the medication. Most patients can not read or understand their prescription, which seems intended to exclude them. In our study we found that:

1. Older adults rely on a network of family members, community members, as well as health care professionals for assistance with learning about medications, and managing them.
2. While older adults continue to perceive medical professionals to be the most reliable source of information on prescription medications, pharmacists (not MD’s) are understood to be both the most reliable and accessible source of information regarding them. Pharmacists are often the only people who discuss ‘side effects’ and warn against taking medications with certain foods.
3. Many seniors shared with us their ambivalent feelings about medications. While grateful that medications exist and can address their illnesses, they also expressed negative feelings towards the fact that they actually have to take them. They just seem to ‘get in the way’ of living a relatively normal life.
4. Many also expressed a desire to take less prescription medication than they do currently. Generally, they think that less medication is better for health, and that only a minimum necessary amount of medication should be taken to address health concerns.
5. Prescription medications are perceived by seniors as serious; most participants in our pilot study said they would not adjust, alter, or stop taking prescription medications without the consent of their physician (though apparently, some do).
6. Prescription medications are understood to be mechanisms of control that regulate specific body parts and functions, but beyond this there was very little knowledge about how they actually work—again, this was seen as belonging to the realm of ‘expert knowledge’ from which they were largely excluded.
7. Many questioned the necessity of all the medications they are currently prescribed, and whether their body truly requires them. Many feel that preventative measures to promote health are not emphasized enough in the Canadian health care system.
8. Many also think that mandatory, frequent screening to test the effectiveness of prescription medications could help reduce the number of medications that they must take.
These findings both support the need for a larger scale health promotion project to deal with ADRs in our region, and they provide us with an idea of the kinds of experiences, attitudes, beliefs and motivations among seniors that we must work with when creating one. Basically, the seniors we interviewed seem motivated to reduce medication where possible, lack information and knowledge about ADRs and defer to most forms of medical authority. This means that to be effective any campaign designed to reduce ADRs will require a serious and broad form of coordination and cooperation with both pharmacists and physicians and should probably include community-based forms of nursing care.

END NOTES

1 This may be a volatile oil, an alkaloid, iridoid or a sesquiterpene. A range of physiological responses occur following stimulation of the bitter receptors of the tongue. The taste of bitterness is transmitted by specific taste buds at the back of the tongue to the central nervous system, triggering a number of reflexes which alter digestion, the endocrine system, immune system responsiveness and the nervous system itself. Fungi living in clay often have antibiotic properties because they produce an array of chemicals to eliminate their competitors for food found in nutrient and mineral rich soil and clay. Likewise, insects have evolved to produce many compounds meant to eliminate or drive away competitors (both plants and other insects) from nutrient sources.


5 For a review of pain in cross cultural contexts, see Free, Mary Moore, “Cross-cultural conceptions of pain and pain control”, Proceedings of Baylor University Medical Center. 2002 April; 15(2): 143–145.


8 These data are for 2005. http://health.howstuffworks.com/10-most-profitable-drugs.htm


For example, some drugs which work as sedatives yield hyperactivity in children and greater anxiety in adults; some antidepressants quite disturbingly result in suicidal compulsions; antipsychotic medications may also aggravate psychotic experiences, and some pain medications actually increase pain in some individuals—resulting in higher doses and worse pain in a terribly vicious cycle. These are widely known, but rarely communicated to patients.


This just means the researchers wait for the outcome, as compared with a retrospective study where the outcomes are known and their causes are what are generally sought.

For a popular summary of this, see Shepherd, Rose, “The Death of the Magic Bullet” *The Sunday Times*, July 31, 2005. Available on line at : (http://www.timesonline.co.uk/tol/life_and_style/article546599.ece?token=null&offset=0&page=1)

According to a survey conducted for the American Society of Health-System Pharmacists (ASHP), 51% of American adults take two or more medications per day, which include over-the-counter drugs. The study also showed that 46% take at least one prescription medication daily and 28% take multiple prescription drugs per day. These figures show that the majority of the adult population in the United States uses drugs of some kind.. As expected the elderly have the highest rate of medication usage with 79% of those over...
65 reported to be taking at least one medication daily. Americans who are over 65 and take medications take an average of 4 medications per day per person.

http://www.chiropracticresearch.org/NEWS_americans_take_more_drugs.htm

27 Bergob, M. Drug use Among Senior Canadians. Canadian Social Trends, Statistics Canada, Ottawa, No. 33, Summer 1994, 26, Catalogue 11-008E

28 Angus Reid Group Inc. Medication use in Canadians aged 55 and older: Opinions and Attitudes, prepared for the Canadian Coalition on Medication Use and the Elderly, 1991


32 “A pilot study of seniors' experiences with medication” Interviewers Ann Holroyd (Nursing, VIU); Britt Vegsund (Anthropology, UVIC). CO-I’s Roseanne Beuthin (Quality Improvement Consultant, VIHA), Elaine Gallagher, UVic (COAG). Peter H. Stephenson was the PI.

Appendix I

“Medicine makes people ill, mathematics makes them sad, and theology makes them sinful”

-Martin Luther-

Common prescription drug interactions with other prescription drugs

■ Mixing anti-diabetic medication and beta blockers can result the decreased response of the anti-diabetic drug and increased frequency and severity of low blood sugar episodes.

■ Mixing anti-diarrheal medication and tranquilizers, sedatives, or sleeping pills can result in an increased effect of tranquilizers, sedatives, or sleeping pills.

■ Mixing antihypertensive medication and digitalis can result in abnormal heart rhythms.

■ Mixing anticoagulants and sleeping pills can result in decreased effectiveness of the anticoagulant medication.
Common over-the-counter (OTC) drug and prescription medication interactions.

■ Aspirin can significantly increase the effect of ‘blood thinning’ drugs (anticoagulants), thus increasing the risk of excessive bleeding.

■ Antacids can cause ‘blood-thinning drugs’ (anticoagulants) to be absorbed too slowly for them to be effective.

■ Antacids can interfere with drug absorption of antibiotics thereby reducing the effectiveness of the drug in fighting infections.

■ Antihistamines, often used for allergies and colds and sometimes as a sleep aid, can increase the sedative effects of barbiturates, tranquilizers, and some prescription pain relievers.

■ Decongestants in cold and cough medications can interact with diuretics (often called “water” pills) to aggravate high blood pressure.

■ Iron supplements taken with antibiotics can reduce or stop the ability of the antibiotics to actually fight infection. (The chemicals in the supplement and the antibiotic bind together in the stomach, instead of being absorbed into the bloodstream.)

■ Salt substitutes can interact with diuretic (‘water’ pills) or blood pressure medication to increase blood potassium levels. This can result in symptoms of nausea, vomiting, muscle cramps, diarrhea, muscle weakness, and even cardiac arrest.

OTC drug interactions with other OTC drugs.

■ Taking a cough medication which contains alcohol at the same time as an antihistamine medication can increase drowsiness and greatly decrease alertness.

■ Mineral oil taken with fat-soluble vitamins (A, D, E, K) reduces the absorption of the vitamins.

Drug and food Interactions

When drugs and certain foods are taken at the same time they can interact in ways that diminish the effectiveness of the ingested drug or reduce the absorption of food nutrients. Additionally, vitamin and herbal supplements taken with prescribed medication can result in some serious adverse reactions; these include:

■ Food can speed up or slow down the action of almost any medication.
Impaired absorption of vitamins and minerals in the body takes place depending on whether they are water or fat soluble.

Either stimulation or suppression of the appetite often occurs.

Drugs can alter how nutrients are actually used in the body.

“Herbs” are often potent, and so they may interact with anesthesia, pain medications, beta-blockers, and anticoagulants. Common plant based medications that are recommended as alternatives to prescription medications can perform similarly to prescription medications. This means that taking both can cause serious problems.

Foods containing active substances that work against certain medications can produce unexpected or adverse effects. If you are taking medication, the food you eat or the supplements you take can actually cause the medication to work incorrectly and in unexpected ways. It’s a good idea to check with your pharmacist about how different foods might affect the medications you take. Some factors affecting the extent of interaction between foods and medications depends on a number of factors including:

- The dosage of the drug.
- A person’s sex, age, size and state of health.
- The time of day that a food is consumed and the time the medication is taken.