MEDICATIONS AND THE ELDERLY

Age, in and of itself, creates changes in cellular metabolism, cellular health, and often times a variety of disease processes. As we age, normal changes occur which impact the absorption and bioavailability and elimination of drugs. Some of the "normal" changes include:

- decrease in small bowel surface area
- increase in gastric pH
- total body water and lean body mass are reduced
- body fat is increased
- decrease in serum albumin, hepatic (liver) mass and blood flow
- decrease in renal (kidney) mass and blood flow (mainly in the renal cortex) is significant
- decrease in creatinine clearance begins after age 30 (about 1/3 of the elderly do not experience this decrease)
- serum creatinine levels remain within normal limits because older persons have less lean body mass, and produce less creatinine
- decreases in tubular function (kidney) are parallel to decreases in glomerular function
- changes occur in drug-receptor interaction, postreceptor events or in adaptive homeostatic responses
- increased organ pathology (disease)

Because of these changes, especially as renal functions continue to decline, dose of drugs given long-term should be periodically reviewed. For drugs which have very serious side effects, such as warfarin, morphine, ACE inhibitors, diazepam, and levodopa, use in the elderly must be approached with caution. Toxicities can occur in some drugs because of reduced effectiveness in the elderly, with a cumulative "side effects" even though the intended effect is reduced. Signs of toxicity may be quite delayed.

Nearly one-third of drug-related hospitalizations and one-half of drug-related deaths occur in persons over the age of 60.[1] There is a demonstrated risk of toxicities with certain drugs:

- long-acting benzodiazepines
- NSAIDs (non-steroidal anti-inflammatory drugs)
- warfarin
- heparin
- aminoglycosides
- isoniazid
- high doses of thiazides
- antineoplastic drugs
- most antiarrhythmic drugs

The risk of adverse drug-drug or drug-disease interaction occurs with aging for a number of reasons. In aging, more diseases occur which may lead to more use of different types of drugs. Some of the drugs may actually interfere with each other, or, worsen a disease. With the complexity

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[1]The Merck Manual, Seventeenth Edition, page 2603.

of diseases and drugs, determining the subtle adverse reactions may be difficult. Some drugs aggravate existing conditions:

- anticholinergic drugs may increase prostatism
- diuretics may increase risk of postural hypotension
- concurrent use of anticholinergics such as antiparkinsonian drugs (benztropine), tricyclic antidepressants (amitriptyline), antipsychotics (thioridazine), and OTC antihistamines (diphenhydramine) may cause or aggravate dry mouth, gum disease, urinary retention, constipation, blurred vision and delirium

Dose requirements for elderly people usually can be reduced. In general, this reduction may be as much as ½ the usual adult dose. Typically, elderly are most likely to under-dose themselves when self-administering medications.

Drug Classes of Concern - The following are drug classes that pose particular risk for older people.

Diuretics. Risk of hypokalemia and hyperglycemia is greater in elderly. Lower doses may help prevent these conditions and reduce the need for potassium supplements.

Antihypertensives. Cardiovascular complications occur with some drug therapies. Complications such as COPD (chronic obstructive pulmonary disease) and PVD (peripheral vascular disease) may contraindicate beta-blockers. In general safe use of diuretics and beta-blockers is preferable.

Antiarrhythmics. Generally these are similar in effectiveness as in younger people. However, because of the altered pharmacokinetics, the does of some should be reduced in the elderly. Risk of significant adverse reactions should be anticipated with increase in age. Digoxin clearance decreases and average of 50% in elderly persons with normal serum creatinine levels, therefore maintenance doses may be started at a lower (0.125 mg/day) level.

Antiparkinsonian drugs. Clearance of levodopa is reduced in older persons, who are also typically more susceptible to postural hypotension and confusion. Careful monitoring and lower starting doses are usually indicated.

Anticoagulants. The effect of warfarin products may be increased because of greater sensitivity, even though the actual pharmacokinetics is not different for the elderly. Also, when withdrawn, such as for surgical procedures, the return to normal clotting status may be slower for older patients.

Psychoactive drugs. Antipsychotics only marginally control agitation in the elderly, non-psychotic person. They may worsen confusion even though they may reduce expressed paranoia. Tardive dyskinesia is an especially big concern, for women more so than men, because it can be irreversible. Side effects such as sedation,

hypotension, akathisia (inability to sit down because the thought of doing so causes severe anxiety; feeling of restlessness and an urgent need of movement; may feel muscular quivering) can occur in 20% of those taking antipsychotic drugs. Drug-induced Parkinsonism can persist for 6-9 months after stopping the drug.

Anxiolytic and hypnotics. Other causes and treatments for insomnia should be investigated before using hypnotics. Limited time use of these drugs is advisable because of issues of toxicity, tolerance, dependence and possible rebound insomnia and anxiety when they are withdrawn.

Antidepressants. Selective serotonin reuptake inhibitors (SSRI) are generally useful and relatively safe. They seem to produce less toxicity even in overdose. Long-elimination half-life of some of these drugs may make some problematic because of active metabolites. Paroxetine is more sedating and can inhibit liver enzyme activities, creating a risk of impaired metabolism of other drugs. Tricyclic antidepressants are effective, but may have anticholinergic adverse effects. Overdose of norepinephrine reuptake inhibitors produces cardiac and neurologic toxicity, and should not be used with those at risk of suicide.

Hypoglycemics. Aging can reduce insulin clearance, but dose requirements are based upon the level of insulin resistance, which varies considerably in type II diabetes. Hypoglycemic reactions may increase with age in those using sulfonylurea. Some newer agents, such as metformin, have demonstrated effectiveness but long-term safety has not yet been established for elderly persons. Renal insufficiencies may increase the risk of lactic acidosis.

Analgesics. Decreased clearance of salicylates, oxaprozin, and naproxen may be a contraindication for using these drugs. Peptic ulcer disease and upper GI bleeding are serious side effects which should be considered in selecting analgesics. Risk of upper GI hemorrhage increase more than 10 times when NSAIDs are combined with warfarin. Gastric acid changes in aging may contribute to the intolerance or potential for adverse reactions. Risk for NSAID-induced renal impairment may be increased for elderly. Monitoring of the serum creatinine may help especially if the person has other diseases such as heart failure, renal impairment, cirrhosis with ascites, diuretic use).