# UNIT 4 PHARMACOKINETICS AND PHARMACODYNAMICS

**Structure**



## 4.0 OBJECTIVES

After studying this unit, you should be able to:

- recognize the change in body physiology that may affect drug response;
- identify different pharmacokinetic factors that cause altered drug responsiveness;
- list different pharmaco dynamic factors that may be changed in elderly;
- individuals at high risk of developing side effects and drug interactions; and
- enumerate the drugs that need specific caution while prescribing for elderly patients.

## 4.1 INTRODUCTION

While an absolute definition of 'elderly' does not exist, most epidemiological and physiological studies have continued to use the cut-off point of 65 years of age for this definition.

It is now generally accepted that the world is experiencing a "demographic revolution" —the population of the world is aging. On account of this shift in population demographics, there is an increasing proportion (more than 12%) of individuals aged over 65 years in the general population. In fact, the fastest growing group of people is the cadre over age 85.

World Health Organization has estimated that between the years 1980 to 2000, there will be about 100 million people over 65 years in the developing countries as against about 38 million in developed countries. With the large total population in India, the elderly people in the country are projected to increase to about 61 million by the end of this century.

As the elderly segment of our population expands, physicians will be prescribing medications more frequently for this age group. Chronic disease is common among older adults. Hence, it is not surprising that both the frequency of drug therapy and the average number of drugs taken per person increases with age. Aging has been described as a progressive decrease in adaptive capacities, such that regulatory mechanisms are easily disrupted stressors to the system, including drugs, may lead to unexpected or unpredictable responses.

Typically, drug therapeutic evaluations are stratified across all age groups within the population of a given disease, and specific impact of either established or newer therapies upon the elderly population is often not readily available. Most of our scientific understanding of

therapeutics, clinical pharmacology and pharmacokinetics is based on studies in young people, whereas, our approach to therapeutics in the elderly patient is often based on anecdotal data, clinical impression and trial and error.

Pharmacological responses are altered with age and adverse drug reactions occur more frequently in elderly patients. Older patients often have multiple chronic diseases that require concurrent medications. In addition, the effects of standard doses are difficult to predict because organ function and pharmacological responses are more variable among individuals as age increases.

**Increased drug use, decreased predictability of response and increased susceptibility to adverse reactions are among the factors that complicate drug therapy in elderly patients.**

Two principal conceptual approaches to the problem of predicting quantitative and qualitative changes in drug sensitivity in the geriatric population are: (i) the pharmacodynamics, and (ii) the pharmacokinetics. As an aid to prescribing appropriately for the elderly it is pertinent to first discuss the significant changes associated with aging. The disposition of drug therapy in elderly patients can be affected by several mechanisms such as, pharmacodynamic alteration in drug handling due to change in organ systems and effects that relate to altered pharmacokinetics. Such changes are many and encompass the absorption, distribution, metabolism and excretion of drugs. These will be discussed in detail as this concept lies within the framework of this unit.

## 4.2 ALTERED DRUG RESPONSIVENESS IN ELDERLY PATIENTS

It has been evidenced that a linear decrease in functional capacity of major organ systems begins at 45 years of age. There is no middle age plateau, specific functions do not decline at an accelerated rate in elderly, but there is progressive decline in many parameters of physiological function which may influence the disposition of drugs in geriatric patients (Tables 4.1 and 4.2).

**Table 4.1: Changes in Body Composition in the Eldely**

- Decline in total body size
- Decline in lean body mass
- Increase in body fat stores
- Decline in total body water
- Decline in liver mass
- Decline in kidney mass

**Table 4.2: Changes in the Gastrointestinal Tract in Old Age**

- Reduction in gastric acidity
- Decreased gastric emptying
- Increased intestinal transit time
- Decreased absorption surface
- Reduced gut blood flow
- Possible reduction in gastrointestinal active transport
- Reduction in liver size
- Reduction in liver blood flow

The intensity and duration of drug action is determined mainly by the concentration of unbound drug at site of action, which in turn is related to drug absorption, distribution and elimination. Although absorption does not change with age for most drugs, distribution and metabolism or elimination may be altered. Therefore, decision concerning the optimal dosage

in relation to physiological age-related changes of liver and kidney function in conjunction with other structural changes merit careful consideration. In addition the physiological response to a standard drug concentration and the homeostatic response to a pharmacologically induced stress may be altered in elderly patients. Thus, changes in pharmacokinetics and end organ response may predispose elderly patients to adverse drug reactions.

**Variability between individuals increases with age, hence drug therapy must be individualised in each elderly patient with careful monitoring of therapeutic effectiveness and attention of the development of adverse effects.**

## 4.2.1 Pharmacokinetic Factors

### Drug Absorption

The amount of drug that reaches the systemic circulation (bioavailability) following oral drug administration depends on gastrointestinal absorption and presystemic metabolism during its first passage through the gastrointestinal mucosa and the liver. The changes in gastrointestinal tract with aging are summarized in Table 4.2.

The absorption of substances that are actively transported from the intestinal lumen including some sugars, minerals and vitamines may, therefore, be decreased in elderly patients. However, most drugs are passively absorbed and although the rate of absorption may be slightly decreased, major alterations with aging have not been identified.

Concurrently administered antacids decrease the absorption of drugs such as chlorpromazine, tetracycline, cimetidine, isoniazid and penicillamine, while cholestyramine binds and decreases the absorpion of many drugs including thiazides, phenobarbital, anticoagulants, digitalis glycosides, acetylsalicyclic acid (aspirin), paracetamol and penicillin. Thus, although major changes in drug absorption from age alone have not been identified, the effects of disease and concurrent drug therapy may be important. Following absorption, drugs pass through the portal system to the liver. Agents such as propranolol and the nitrates are subject to significant first pass hepatic extraction which reduces their bioavailability. With aging such hepatic extraction may be altered. e.g. increased plasma concentrations of propranolol following oral administration in elderly patients may be related to decreased hepatic extraction.

### Drug Distribution

Drug distribution is determined by body composition (Table 4.1), plasma protein binding and organ blood flow. Total body water and body mass decrease with age. Body fat as a percentage of body weight increase with aging until the age of 80-85 years and then decreases. As a result of these changes in body composition, use of standardized drug dosages in elderly patients may be expected to produce higher drug concentrations in the blood. The extent of distribution of a drug is determined by its molecular size, lipophilicity, acid/base properties and binding of the drug to plasma albumin and tissue proteins. The increase in body fat with age and decrease in body water may lead to changes in the apparent volumes of distribution of highly lipid soluble (e.g. diazepam lidocaine) or water soluble (e.g. acetaminophen, antipyrine and ethanol) drugs with age.

The concept of apparent volume of distribution (Vd) is a useful measure at any one time of the amount of drug in the body as a whole, relative to that in the plasma. The prefix 'apparent' clarifies that Vd is a theoretical concept rather than an actual volume. The value of Vd is often different in the young and elderly subjects, for the same drug. Some examples of how this affects interpretation are provided by highly water soluble drugs such as digoxin. The Vd for digoxin is reduced in the elderly as a consequence of reduction in body water and a smaller dose is required to provide adequate digitalization and avoid potential toxicity. Lowered distribution of volume have also been shown for the water soluble drugs, paracetamol and ethanol.

The opposite is true of the lipid soluble drugs such as lignocaine and thiopentone, where, not unexpectedly the volume of distribution rises in old age because of increased body fat. This may lead to an increased half-life of the drug as plasma clearance remains constant. This may result in an increased drug effect and toxicity, which may require dosage reduction.

**Thus, as is clear from the above examples, with few exceptions, the overall effect of changes in Vd can be seen to require reduction the dosage of the drug required by the elderly. Therefore, wherever possible, the practicing clinician should attempt to titrate the lowest possible dose against the desired therapeutic effect.**

Change in organ blood flow with aging may also affect the rate of drug distribution. It has been evidenced that cardiac output decreases and peripheral vascular resistance increases with age. Hepatic and renal blood flow are decreased and an increased fraction of cardiac output is distributed to the brain, heart and skeletal muscle. Although many of these changes are at least partly a result of prior illness, the average elderly patient will probably have altered blood flow compared with younger patients.

**Protein Binding**

Plasma protein binding may be reduced as a result of : (i) reduction in plasma albumin (20% less than the 20 year olds) which is the major binding protein, or (ii) as a result of changes in binding affinity due to aging, leading to an increased free concentration of extensively bound drugs. The significance of these changes in terms of altered drug effects would be negligible but for the concomitant alterations in elimination capacity (metabolism or exertion) in this age group. In fact, it is the possible change in drug elimination capacity that is of most importance in this context. For the majority of protein bound drugs, the free (unbound fraction) is available for pharmacodynamic action, metabolism and elimination. Hence, if through aging, drug interaction, or a renal or hepatic feature, a significant increase in free-fraction results, the pharmacodynamic response would be enhanced.

In contrast, the concentration of alpha acid glycoprotein may be increased in presence of chronic diseases that frequently occur in the geriatric population resulting in increased binding of drugs such as antidepressants, antipsychotic drugs with β-blockers which are mainly bound to this protein. Hence these drugs may be required to be given in higher doses.

**Drug Elimination**

The principal mechanisms of drug elimination are hepatic metabolism and renal excretion. If the drug elimination is decreased, the effects of a single dose are prolonged resulting in the increase in steady-state concentration. This warrants dosage adjuntment, as mentioned above.

**Hepatic Metabolism**

Hepatic blood flow and liver mass change in proportion to body weight and decrease with aging. There is a 40-50 per cent decrease in hepatic blood flow in elderly as compared with young adults. These changes may alter the ability of the liver to metabolize drugs.

The ability of the liver to metabolize drugs does not decline similarly for all drugs with advancing age. The most frequent change involves the microsomal mixed-function oxidative system (Phase I reactions: oxidation and reduction), but little or no change occurs in the conjugative processes (Phase II reactions: conjugation) (Table 4.3). Hepatic blood flow declines with age because of reduced cardiac output.

As consequence of reduced metabolism, certain drugs that are cleared by the liver may require administration in lower dosages to avoid accumulation and excessive pharmacologic effect. In general drugs with low hepatic extraction have a high volume of distribution, a reduction in clearance and a prolongation of the elimination half-life. Drugs in this class can be divided into those involving Phase I reactions and Phase II reactions.

**Table 4.3 : Effects of Age on Hepatic Clearance of Some Drugs**

| Age-Related Decrease in Hepatic Clearance Found | No age Difference Found |
|---|---|
| Alprazolam | Ethanol* |
| Barbiturates | Isoniazid |
| Carbenoxolone | Lidocanine |
| Chlordiazepoxide | Lorazepam* |
| Clobazam | Notrazepam* |
| Desmethyldiazepam | Oxazepam* |
| Flurazepam | Prazosin |
| Imipramine | Salicylate* |
| Meperidine | Warfarin* |
| Nortriptyline | |
| Phenylbutazone | |
| Propranolol | |
| Quinidine, quinine | |
| Theophylline | |
| Tolbutamide | |

***Note*:** All the drugs undergo Phase I metabolism by hepatic mixed function oxidase system except those marked with asterik (*) which undergo Phase II metabolism (conjugation) or Phase I metabolsim by non-microsomal systems.

### *Phase I Reactions*

These reactions introduce polar groups into drug molecules by oxidation, reduction, demethylation and hydrolytic processes. The most important of these are the oxidative steps which are carried out by the microsomal mixed function oxidase-drug metabolizing system in the liver parenchymal cell.

It is generally held that the activity of the microsomal mixed function oxidase system declines with age. This conclusion is largely based on studies with antipyrine; because, this drug is used as an index of hepatic metabolism and is an excellent model for studying the microsomal mixed function oxidase-drug-metabolizing system within the liver. In the elderly, a prolongation of antipyrine plasma half-life and a decrease in its metabolism and clearance have been shown.

### *Phase II Reactions*

Non-microsomal enzyme pathways may be less affected by age. Thus, there is little effect of aging on the elimination of isoniazid, rifampicin, paracetamol, lidocaine, valproic acid, salicylate, indomethacin and oxprenolol. However, some studies have shown that the elimination of paracetamol, ketoprofen, salicylate, naproxen and morphine is reduced in elderly patients.

Benzodiazepines that primarily undergo conjugation in the liver and are without active metabolites include oxazepam, lorazepam and temazepam (although oxazepam is a minor metabolite of temazepam). Cumulative or prolonged sedative effects may be less likely with these compunds because they have shorter half-lives and their elimination may be unaltered with age.

Ethanol metabolism by alcohol dehydrogenase and isoniazid elimination by acetylation are unchanged in elderly patients. Although it is controversial whether drug acetylation is altered with age; a large study in healthy volunteers did not demonstrate a clinically important effect of age or gender.

Concurrent drug administration, illness, genetics and environmental factors including smoking may have more important effects on drug metabolism than age. It has been reported that causes of enzyme induction such as smoking may have less effect in elderly than in young patients, however, data evidencing this is not entirely consistent. In contrast, drugs that

decrease microsomal enzyme activity such as cimetidine may potentially exacerbate age-related changes, however, the inhibitory effects of the drug do not differ with age.

*Renal Excretion*

Most drug are excreted predominantly by the renal route, although some like digoxin also enter an enterohepatic cycle. Renal excretion is dependent upon the renal blood flow, glomerular filtration rate, and tubular function all of which decline with age. Between the ages of 20 and 90 years, there is an average decline of 35 per cent in glomerular filtration rate. However, muscle mass causes a decrease in endogenous creatining production so that serum creatinine concentrations remain within normal ranges and do not reflect the decrease in creatinine clearance. Renal tubular function deteriorates with age as the absolute number of nephrons declines and may affect in particular the elimination of drugs which are actively secreted in the nephron. In addition to the physiological decline in renal function the elderly patient is particularly liable to renal impairment due to dehydration, cogestive heart failure, hypotension and urinary retention or to intrinsic renal involvement e.g. diabetic nephropathy or pyelonephritis.

An age-related decrease in excretion of most drugs correlates with altered renal function. This may lead to the accumulation of some drugs with age (Table 4.4). Drugs with significant toxicity that have diminished renal excretion with age due to the decline in the glomerular filtration rate include allopurinol, aminoglycosid, amantadine, lithium, digoxin, procainamide, chorpropamide penicillin, and cimetedine. These agents may have reduced clearance, prolonged half-lives and increased steady-state concentrations if dosages are not adjusted for renal function.

**Table 4.4 : Drug Accumulation Due to Diminished Renal Excretion in Old Age**

| Drug | Clinical Correlations |
|---|---|
| Lithium | CNS toxicity, renal toxicity, inappropriate ADH syndrome |
| Cimetidine | Sedation, gynaecomastia, confusion |
| Digoxin | Cardiac toxicity, confusion, vomiting |
| Gentamicin | Ototoxicity, renal toxicity |
| Co-trimoxazole | Bone marrow toxicity |
| Penicillin | Little effect |
| Tetracycline | Renal toxicity |

## 4.2.2 Pharmacodynamic Factors

**Age-related Changes**

In addition to changes in the pharmacokinetic factors that may alter unbound drug concentrations, organ response and homeostatic counter regulation may be altered with aging. Responses to drugs in the elderly patients may be accentuated or modified by age related changes in homeostatic responses such as postural control, orthostatic circulatory responses, thermoregulation, visceral mass function and cognitive function.

Sites of drug action include cell surface receptors, intracellular receptors, enzymes and membrane ion channels. In the case of receptor agonists, tissue response is dependent on receptor binding, intracellular stimulus response coupling and activation of effector mechanisms. The physicological response includes both the direct drug effect and the homeostatic responses of that pharmacological effect. Furthermore, decreased homeostatic ounter-regulation with aging may be a significant cause of adverse drug reactions.

**Receptor Sensitivity**

Beta-adrenoceptor mediated effects are altered with aging. The decrease in beta-adrenoceptor response is due to a reduction in high affinity binding sites and altered post-receptor mechanisms

resembling desensitization. It should be noted that the cardiovascular system is one of the most important organ systems in which uspronsimeners decreases with age. Evidence that beta-adrenoceptors are aldered with aging is not well established.

Elderly patients are known to be oversensitive, psychotropic drugs; e.g., psychomotor manifestations of benzodiazepines occur at lower concentrations in elderly than in a young adult. These altered responses have been demonstrated with nitrazepam and diazepam. However, it has been observed that these changes are likely to be due to a combination of increased tissue sensitivity, decreased ability to compensate for altered CNS function and altered pharmacokinetic factors.

Inter-individual variation in most physiological parameters also increases with age and drug effects may be difficult to predict. Because unpredictable sensitivity to drug effects are common, initial doses should be low and the final dose adjusted according to individual tolerability.

Central nervous system (CNS) adverse effects including confusion, disorientation, agitation or sedation are common in elderly patients with tricyclic antidepressants, phenothiazines, anticholinergic drugs, barbiturates levodopa and cimetidine.

**Impaired Homeostasis**

A common factor underlying all research into aging, including pharmacodynamics, is that of a progressive fall in homeostatic reserve or the loss of capacity to adapt to therapy. This principle is expressed through the reduced efficiency of the various mechanisms which normally counter-balance the effects of a variety of drugs. Impaired homeostasis is a frequent cause of adverse drug effects. e.g. elderly patients have an impaired ability to excrete free water load. Hence, administration of hydrochlorothiazine further impairs free water excretion, rendering the patient at risk of dilutional hyponatremia. Volume depletion is also a risk. While the senescent kidney is able to decrease urinary sodium to low concentrations, the adaptive response is delayed and extracellular fluid loss may be significant during this period. Volume depletion is further exacerbated by diminished plasma renin activity, the basal level of which is decreased by 30 per cent to 50 per cent in elderly patients.

Postural hypotension is frequent in elderly individuals and may be exacerbated by many drugs. The pathogenesis is multifactorial and includes decreased barorceptor response, altered sympathetic activity and responsiveness, impaired vasomotor response in both arterioles and veins, and altered volume regulation. Drugs that alter CNS function, sympathetic activity, vasomotor response, cardiac function or volume regulation may exacerbate postural changes in blood pressure. Phenothiazines, tricyclic antidepressants, levodopa, antihypertensive drugs and diuretics are frequent causes of postural hypotension.

**Check Your Progress 1**

1) What are the alterations in the physiological systems of an elderly which affect response of drugs as compared to those in adult individuals?

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2) What are the major pharmacokinetic factors that cause altered drug response?

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3) Enumerate different pharmacodynamic facts that may be altered in the body of an elderly individual?

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## 4.3 ADVERSE DRUG REACTIONS

The positive relationship between number of drugs taken and the incidence of adverse reactions to them has been well documented. In long-term care facilities, which have a high population of the elderly, the average number of prescriptions per patient varies between 6.6 and 7.7. Studies have shown that the percentage of patients with adverse reactions increases from about 10 per cent when a single drug is being taken to nearly 100 per cent when ten drugs are taken. Thus, it may be expected that about half of patients in long-term care facilities will have recognized or unrecognized reactions at some time. The overall incidence of drug reactions in geriatric patients is estimated to be at least twice that in the younger population. Reasons for this high incidence undoubtedly include errors in prescribing on the part of the practitioner and errors in drug usage by the patient.

Practitioner errors sometimes occur because the physician does not appreciate the importance of changes in pharmacokinetics with age and age-related diseases. Some errors occur because the practitioner is unaware of incompatible drugs prescribed by other practitioners for the same patients. e.g., cimetidine, a drug heavily prescribed to the elderly, has a much higher incidence of untoward effects (e.g. confusion, slurred speech) in the geriatric population than in younger patients. It also inhibits the hepatic metabolism of many drugs, including phenytoin, warfarin, beta-blockers, and other agents. A patient who has been taking one of the latter agents without ill effect may develop markedly elevated bood levels and severe toxicity if cimetidine is added to the regimen without adjustment of dosage of the other drugs.

Patient errors may result from non-compliance. In addition, they often result from use of nonprescription drugs that are taken without the knowledge of the physician. Many OTC agents contain "hidden ingredients" with potent pharmacologic effects. e.g. many antihistamines have significant sedative effects and are inherently more hazardous in patients with impaired cognitive function. Similarly, their antimuscarinic action may precipitate urinary retention in the geriatric male or glaucoma in a patient with a narrow anterior chamber angle. If the patient is also taking a metabolism inhibitor such as cimetidine, the probability of an adverse reaction is greatly increased.

### 4.3.1 Practical Aspects of Geriatric Pharmacology

The quality of life in elderly patients can be greatly improved and life can be prolonged by the intelligent use of drugs. However, there are several practical obstacles to compliance that the prescriber must recognize.

The expense of drugs can be a major disincentive in patients receiving marginal retirement incomes who are not covered by health insurance. The prescriber must be aware of the cost of the prescription and of cheaper alternative therapies.

Non-compliance may result from forgetfulness or confusion, especially if the patient has several prescriptions and different dosing intervals. Since the prescriptions are often written by several different practitioners, there is usually no attempt to design "integrated" regimens that use drugs with similar dosing intervals for the conditions being treated. Patients may forget instructions regarding the need to complete a fixed duration of therapy when a course of anti-infective drug is being given. The disappearance of symptoms is often garded as the best reason to halt drug taking especially if the prescription was expensive.

Non-compliance may also be deliberate. A decision not to take a drug may be based on prior experience with it. There may be excellent reasons for such "intelligent" non-compliance and

the practitioner should try to elicit them. Such efforts may also improve compliance with alternative drugs, because enlisting the patient as a participant in therpaeutic decisions tend to increase the motivation to succeed.

Some errors in drug taking are caused by physical disabilities. Arthritis, tremor, and visual problems may all contribute. Liquid medications that are to be measured out "by the spoonful" are especially inappropriate for patients with any type of tremor or motor disability. The use of a pediatric dosing syringe may be helpful in such cases. Because of decreased production of saliva, older patients often have difficulty swallowing large tablets. "Childproof" containers are often "patient-proof" if the patient has arthritis. Cataracts and macular degeneration occur in a large number of patients over 70; therefore, labels on prescription bottles should be large enough for the patients with diminished vision to read, or colour-coded it the patient can see but can no longer read.

### 4.3.2 Polypharmacy

Polypharmacy, i.e. prescription of multiple drugs, is very common in the elderly population. It has been associated with poor drug compliance and increased adverse drug effects causing morbidity, mortality and hospital admissions. Hospitalization of a patient may further contribute to the problem of polypharmacy. Studies have shown that the average number of medication per elderly patient is between 4 and 5, which increases during hospitalization. The trend towards medication increase suggests that patients have drugs added to their list for acute medical problems and drugs are more often substituted than omitted.

## 4.4 PRESCRIBING FOR THE ELDERLY PATIENT

In view of the problems associated with polypharmacy, a more conservative approach to medication review may need to be considered. Finally, all doctors treating elderly patients should critically assess drug lists and withdraw drugs which are no longer indicated. This is of concern since this population is more vulnerable to the adverse effects of polypharmacy.

Basic principles of prescribing for the elderly patient to be considered before initiating drug therapy are as follows :

- Is drug therapy required?
- If drug treatment is required, which drug is appropriate?
- Is the patient being asked to take more drugs than are tolerable or manageable?
- Which type of preparation should be used?
- Should the standard dosage be used, or the dosage schedule modified?
- Which adverse effects are likely to occur and which drugs should be avoided, if possible?
- Can the elderly patient living alone manage self medication?

These edicts do not mean, however, that drugs should be withheld on account of old age, particularly when appropriate drug treatment can improve the quality of life of the elderly patient. Hence, it is recommended hat cautious prescribing is essential to minimize the likelihood of provoking reactions. However, the elderly should not be denied the benefit of new drugs when indicated and the physician must be aware of the correct dosage and the pharmacokinetic changes due to changed body composition resulting in water soluble drugs having a decreased, and liposoluble drugs an increased, effect in the volume of distribution. Hepatic catabolism of drugs is slower due to decreased hepatic blood flow. Bioavailability is often increased because of reduction in first pass metabolism. The rate of renal elimination is lower because of decreased renal function. The overall results are of adverse reactions being more common and sequelae more severe.

**Check Your Progress 2**

1) It is generally considered that drugs may produce increased side effects in elderly individuals as compared to those in adult individuals, comment.

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2) Most elderly individuals use number of drugs at the same time in order to control the number of morbidities. Explain the risks of such practice?

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## 4.5 LET US SUM UP

With an increase in the life span, morbidities among the elderly shall also increase. These will warrant increase in the prescribing drugs. You have learnt that with an increase in age, there is a progressive decline in many parameters, which influence the disposition of drugs in geriatric patients. These factors include changes in body composition and gastrointestinal tract. Inspite of these factors, variability between individuals increases with age and hence drug therapy must be individualised with careful monitoring.

Adverse reactions to drugs in the elderly is another aspect that requires attention. The overall incidence of drug reactions is geriatric patients is estimated to be at least twice that in the younger population. Incompatibility of various drugs must be kept in mind while prescribing. You must be careful to ask if the patient is being treated for any other acute or chronic illness.

## 4.6 KEY WORDS

**Adverse drug reaction (ADR)** : Severe reaction which takes place after taking drug which might be fatal in nature.

**Aging** : Process of deterioration in the functional capacity of a person and resulting in structural changes.

**Antacids** : Which neutralises the excess Acid in the stomach.

**Anti depressants** : Drug which improve depression.

**Chronic disease** : Disease of long standing nature which have effect on organ system.

**Orthostatic hypotension** : Fall of blood pressure on standing.

**Poly pharmacy** : Uses of more than two drugs at a time.

**Rental Toxicity** : Drug which cause impairment of Kidney function.

## 4.7 ANSWERS TO CHECK YOUR PROGRESS

**Check Your Progress 1**

1) Alterations in Physiological system of an elderly which affect response to drugs are:
   1. Decline in total body size
   2. Increase in body fat stores
   3. Decline in total body water
   4. Decline in liver mass
   5. Decline in kidney mass

2) Major Pharmaco-kinetic factors are:
   1. Drug absorption and bio-availability
   2. Drug distribution
   3. Organ blood flow
   4. Plasma protein binding
   5. Drug metabolism
   6. Drug excretion

3) Different Pharmecodynamic factors are; Age related changes, Receptor sensitivity and impaired homoestasis.

**Check Your Progress 2**

1) Yes. Over all incidence of drug reaction is at least twice that in the young because of lack of knowledge about changes in Pharmaco-kinetics associated with age and age related diseases and drug inter actions.

2) Poly Pharmacy is associated with poor drug compliance and increase drug reactions.