The Effects of Medication on Cognition in Long-Term Care

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ABSTRACT

This article emphasizes the need to consider the role of medications when providing speech-language pathology services to a person with cognitive decline. This is particularly true when working with older adults. Many older adults take multiple medications that may have a direct effect on cognitive ability and as a result, on the success of rehabilitation efforts.

KEYWORDS: Polypharmacy, neurotransmitters, benzodiazepines

Learning Outcomes: As a result of this activity, the reader will be able to (1) identify the relationship between cognitive abilities and polypharmacy; (2) describe the relationship between the speech-language pathologist and physician; (3) explain the importance of a correct diagnosis and accurate staging when examining the cognitive function; (4) discuss the importance of understanding adverse drug reactions and side effects; (5) identify the role of classes of medication such as benzodiazepines to sedation.

The word cognition comes from Latin and means “to know.” Cognition is commonly thought to include memory, attention, learning, problem solving, decision making, reasoning, and language. Several of these cognitive processes may be impaired in individuals who are in long-term care. Therefore, cognitive rehabilitation may play an important role in isolating and identifying drugs that can either improve or disrupt cognitive abilities. In most instances, however, medications are more likely to interfere with, rather than improve, cognition. This is particularly true for the elderly in long-term care settings. Cognitive skills are the underlying skills and mental capacities needed to process and learn information, read and remember, solve problems, and think. Cognitive skills develop and change over time.

This article will discuss the effect of medications on cognition and subsequently on cognitive therapy. The importance of having the correct diagnosis and staging level will be emphasized. The article will also discuss the clinician’s role in identifying medications that may affect cognitive functioning. Finally, general classes of
medications will also be discussed in relation to their effect on cognition.

The first thing to consider when examining the cognitive patterns of older adults is their diagnosis. Frequently, individuals living in long-term care settings manifest some form of dementia. Dementia describes a group of brain disorders that cause loss of memory and other cognitive abilities. It is not a disease itself, but a group of symptoms that characterize several diseases and conditions. Each type of dementia has particular cognitive patterns that can then be influenced by medications. As such, accurate and early diagnosis of the dementia type is important for informing its management. Each dementia type has distinctive patterns of behavioral difficulties, memory loss, and other cognitive strengths and weaknesses unique to that diagnosis. Impairments in cognition are usually classified as reversible or irreversible. Reversible dementia results from a medicine’s side effects, as well as from infection, delirium, malnutrition and dehydration, depression, and hypoglycemia. In addition, the cognitive impairment may range from mild impairment including age-associated mental decline to severe cognitive disabilities such as those seen in people with frontotemporal dementia or with Alzheimer’s disease (AD), the most common type of dementia in the United States.

People with AD suffer primarily from impaired episodic memory; impaired orientation; reduced attention to task; reduced limits of concentration, planning, and judgment; personality changes; and later, speech and walking disorders. Episodic memory decline is frequently accompanied with visual-spatial-temporal orientation difficulties. Anomia, sensory memory, and working memory are also involved. Generally, the higher-level mental functions are affected first. Disorientation to time and space may occur in the later stages.

Another form of dementia, Parkinson’s disease (PD), generally manifests a slowing of the thought processes as well as difficulty concentrating that leads to confusion. In addition, the person with PD may have difficulty with sensory memory, notably speed of processing and subsequent difficulty with working memory, executive function, and metacognition.

A person with vascular dementia, on the other hand, usually presents with an abrupt onset, somatic complaints, and difficulties in all aspects of sensory memory. Vascular dementia differs from other vascular disorders such as stroke in that, although the onset may appear to be abrupt, it is likely to be the end result of repeated, often unrecognized small strokes. The person with vascular dementia has difficulty with semantic memory, whereas the person with AD has more difficulty with episodic memory. In contrast, a person with Huntington’s disease (HD) will experience deficits in procedural memory, which is considered a spared ability until late in the time course of AD. HD is a neurodegenerative disorder resulting in motor, cognitive, and psychiatric deficits. Differences such as these should be considered when evaluating the effects of medication on cognition.

Staging systems provide useful frames of reference for understanding how a type of dementia may progress, which is helpful for developing treatment plans. However, all stages are artificial benchmarks in a continuous process that can vary from one person to another. Not everyone will experience each symptom, and symptoms may occur at different times in different individuals. One common tool used by health care professionals is the Global Deterioration Scale (also called the Reisberg Scale), which measures the progression of AD. This scale divides AD into seven stages of ability. A score of 1 represents average cognition, a score of 4 represents moderate cognitive decline such as difficulty with complex tasks, and a score of 7 represents severe dementia. Certainly, individuals with significant impairment or those in a more advanced stage will have more difficulty compensating for changes in cognition caused by medications. It is thus essential for clinicians to be able accurately determine the patient’s diagnosis and stage of dementia before trying to determine if the person’s cognitive levels have been affected by medications. Staging is also important as the individual probably will respond differentially to therapy. This will affect the appropriateness of many neurobehavioral rehabilitation strategies. For example, the person in stage three (early confusional) should actively attend to notes placed in front of him.
telling him to follow a certain routine while eating. Persons in stage four are likely only to follow the notes if told that they failed to notice the notes spontaneously and are cued by the caregiver. The person in stage five, however, will probably neither notice the notes nor respond to them even when they are pointed out.

ROLE OF THE SPEECH-LANGUAGE PATHOLOGIST

Speech-language pathologists (SLPs) must be knowledgeable about medications and their effect on cognition for several reasons. First, they must be aware of the patient’s response to medications because, as we have noted earlier, they can affect remediation, not only of cognitive, but of motor functioning as well. Second, it is important for SLPs to understand the optimal timing of medication response. For example, a person with PD should ideally receive treatment by an SLP at a time when the dopamine in her body is at a peak level. Also, SLPs should be aware of when a variety of other therapeutic interventions may be influencing the effectiveness of the medications. Whirlpool sessions may result in a drop in blood pressure that, in turn, may increase the risk of orthostatic hypotension and potential falls.7–9 Because medication-induced delirium has numerous symptoms in common with dementia, medication as the cause for impairment of cognitive abilities should always be ruled out.1,7,8 Adverse drug reactions and drug side effects need to be identified and monitored by the clinician during the rehabilitation process. For example, a combination of some antidepressants and antipsychotic medications can result in increased extrapyramidal symptoms. In addition, new symptoms may represent drug interaction among several medications taken by the patient.10

Most medications have dosage-related side effects, with higher dosages usually associated with higher risk. Adverse effects are more frequent in elderly patients and in particular those with renal or liver dysfunction. It is for this reason that initiation of medication should start with a low dose and only be increased slowly. Adverse reactions associated with impairment in cognition increase with the number of medications taken. Decreases in cognitive functioning may result from activity changes of the neurotransmitters that depress central nervous system (CNS) function, notably dopamine, gamma-amino butyric acid, serotonin, histamine, and acetylcholine.12

PRINCIPLES OF PHARMACOTHERAPY

Pharmacotherapy views medication from a clinical standpoint and is defined as the use of a particular medication to prevent, diagnose, and cure disease. The principles of anatomy and physiology, pharmacology, and pathophysiology are integrated in the study of pharmacotherapy. The study of pharmacokinetics as well as pharmacodynamics represents two subdivisions of pharmacotherapy. Pharmacokinetics looks at how medications are absorbed, metabolized, and eliminated by the body. Pharmacokinetics is essential in predicting medication drug levels as well as predicting how long a medication will take before it reaches its desired level. Pharmacodynamics describes the physiological effects of the medication on the body and describes the medication’s mechanism of action at the cellular level.13–15 Knowledge of pharmacotherapy assists the clinician in better understanding of how a given patient’s medication is causing negative cognitive side effects.

Sedative effects result from several medications such as anticholinergics, antipsychotics, antidepressants, and benzodiazepines. Sedation is especially notable at the initiation of a medication or immediately following a dosage change. Drowsiness usually occurs during the first few weeks and then may disappear. The drowsiness can have a direct effect upon cognition. Sedation that continues to occur after this time period is generally an indication that the dose needs to be changed or that the person is
suffering from a drug interaction. Drug interactions can occur in several different ways. For example, the addition of a second drug may interfere with the first drug’s effect. This is known as an antagonistic effect. On the other hand, the addition of the second drug may enhance the first drug’s effect. This is called potentiation.10

POLYPHARMACY

Polypharmacy is the condition of taking or having been prescribed too many medications. The United States is consuming prescription drugs at an alarming rate. Although the United States represents less than 5% of the world’s population, it consumes nearly 75% of all manufactured pharmaceutical medications. Americans spend an average of $8,200 per year on medications—almost twice that of other nations. The United States ranks 37th in overall health compared with many countries, ranking below many in the Third World.16 Drug interactions are more common in the elderly. An analysis of the frail elderly found that the patients took an average of 15 medications (range 6 to 28), with 8.9 drug-related problems per patient (range 3 to 19).17 It was noted that in many instances, patients were often taking medications that were no longer needed for their medical problems and that these medications were contributing to side effects. Typical medications no longer required have included antihypertensive medications, proton pump inhibitors, and iron.

Drug-related morbidity in the frail elderly can be avoided. Much of the difficulty lies in inappropriate prescribing.18 The elderly experience more age-related changes to the body than younger persons do. The elderly may experience confusion due to polypharmacy combined with visual difficulties, auditory difficulties, and memory impairments. The elderly may also not understand the drug treatment plan, and as a result fail to comply. In addition, the elderly historically have a higher level of polypharmacy due to multiple health problems. Many elderly persons live alone, have difficulty affording their prescriptions, or have difficulty visiting their physician. These challenges can result in medication side effects and thus cognitive problems.18

Older adults have a reduced ability to metabolize and excrete medications. Because of changes in body composition as people age, older people typically have higher levels of body fat than younger people. A decrease in lean body mass and total body water decreases both metabolism and renal function. This results in changes to the volume of distribution of medications that are water soluble. Increases in the medication in the bloodstream contribute to increased effects and toxicity. Brain mass decreases, motor coordination decreases, reaction time slows, and cerebral blood flow decreases, making short-term memory less efficient. The blood–brain barrier is more permeable in the elderly, allowing medications to cross into the CNS, and thereby increasing drug toxicity. Altered mental status is often related to the size of the dose, with higher risk seen in the older person.10

CLASSES OF MEDICATIONS AFFECTING COGNITION

Benzodiazepines

Benzodiazepines are antianxiety medications such as Xanax, Ativan, Librium, and Valium. Benzodiazepines have anticonvulsant, hypnotic, muscle relaxant, and sedative effects. Used judiciously, these medications can enhance the person’s psychological and physical well-being. Altered drug disposition, however, results in the elderly being sensitive to the drug’s side effects. This can lead to psychological and physical decline with the addition of other medications and the risk of drug interaction.19 These medications can result in sedation, confusion, and falls. They also can result in anterograde amnesia. Benzodiazepines also shorten sleep onset and suppress stage four and REM sleep (suppressing dreams). When benzodiazepine therapy is initiated, it is suggested that short-acting medications be utilized. For example, Xanax has a shorter half-life and is preferred over the long half-life benzodiazepines. Long-acting benzodiazepines (such as Valium) can result in profound cognitive impairment, profound confusion, forgetfulness, morning hangover effect, and falls.10,19 All benzodiazepines work to decrease anxiety.
The choice of which benzodiazepine to use depends on rate of onset, rate of elimination, potential side effects, and drug interactions. For example, SLPs need to check medications when working with an elderly person who has dysphagia. This patient may complain of a lack of appetite due to a loss of taste. Benzodiazepines such as Xanax, however, will result in taste loss and lessening interest in food and eating.

Drug interactions with medications such as antacids, chronic obstructive pulmonary disease medications, anti-infective medications, antidepressants, and cardiac medication generally result in decreased benzodiazepine clearance and increased sedation that affects cognition. For example, Valium mixed with alcohol, Prilosec, or Prozac and Xanax mixed with Tagamet will result in decreased benzodiazepine clearance and increased sedation.12

Antidepressants
Depression is a psychiatric illness with symptoms that reflect loss of ability to concentrate or experience pleasure. This disorder also includes apathy, social withdrawal, guilt, and sleep and appetite disturbances. The commonly seen side effects of these medications include changes in heart rate and rhythm, hypotension, and hypertension and sedation. The side effect of sedation associated with antidepressants can result in decreased attention to eating and decreased appetite, especially with therapy initiation or with dosage change. The feeling of drowsiness usually occurs during the first 2 weeks upon medication initiation and then generally diminishes. Sedation that remains after the first several weeks is an indication to consider drug interactions or lowering of dosage.20,21 The tricyclic and tetracyclic antidepressants such as Elavil generally present a high probability of sedation. Selective serotonin reuptake inhibitors such as Prozac, Paxil, Zoloft, and Effexor present with a low probability of sedation. Atypical antidepressants present a mixed picture regarding sedation. For example, Wellbutrin presents a low probability of sedation whereas Remeron and Serzone present a high probability of sedation.21

Antidepressants can result in CNS effects such as agitation, confusion, and sedation. Drug interactions with antianxiety and sleep agents present a mixed drug picture based on the antidepressant. For example, drug interaction between Xanex and Prozac can result in increased sedation. Interaction with Valium and Luvox can also increase sedation. Drug interactions between BuSp and Prozac, however, result in a decreased effect of Prozac.12,20,21

Antipsychotic Agents
Antipsychotic agents such as Haldol, Mellaril, and Thorazine (first-generation) used in the treatment of delusions and hallucinations can result in confusion, sedation, Parkinsonism, and tardive dyskinesia. The sedation effect, however, is mixed, and depends on the particular medication. For example, Thorazine, Serentil, and Mellaril have a high probability of sedation and a low to moderate probability of extrapyramidal symptoms. Haldol and Orap, on the other hand, have a low probability of sedation and a high probability of extrapyramidal symptoms.22,23 Atypical antipsychotics (second-generation) also present a mixed picture of sedation. Dibenzapines (Clozaril, Zyprexa, and Seroquel) demonstrate a high probability for sedation. Benzisoxazoles (Risperdal) present a low probability of sedation, whereas Geodon presents a moderate probability of sedation. Aripiprazole (Abilify) presents a low probability of sedation. Antipsychotic drug interactions with medications that are anticholinergic (antihistamines, tricyclic antidepressants, anti-Parkinson’s agents) will result in decreased antipsychotic effects. Drug interactions with benzodiazepines (Valium, Librium) will result in respiratory depression, ataxia, stupor, and additive sedation.10,12

Antihistamines
Histamine contributes to a local response of inflammation. Subsequently, antihistamines reduce inflammation. Antihistamines (such as Benadryl) are used to treat allergies and sinus problems. Antihistamines can result in sedation and confusion and sleep disturbances. Antihistamines are one of many anticholinergic medications that often cause xerostomia.12 The antihistamine Benadryl syrup (12.5 mg/5 mil
concentration) may be used as a topical with products such as Magic Mouthwash for stomatitis (inflammation of the mucosal lining of the mouth). The side effect, however (if swallowed), is decreased gastrointestinal mobility, constipation, xerostomia, and sedation.24

**Antiemetics**

Antiemetics used for nausea relief such as Phenergan will also result in confusion, sedation, Parkinsonism, and tardive dyskinesia.

**Analgesics**

Analgesics used in pain relief such as Darvon can also result in confusion and sedation.18

**Prolonged Use of Medications**

Regular use of psychiatric drugs, antihistamines, and pain medications can result in cognitive decline and memory loss. For example, anticholinergics function to block the neurotransmitter acetylcholine. Acetylcholine is one of the main neurotransmitters responsible for memory and cognition. The difficulty with anticholinergic medications is that they are cumulative. The physician may not be aware of all of the anticholinergic medications in the patient’s drug regimen. People taking at least one anticholinergic medication scored lower on cognitive functioning measures than those subjects not receiving anticholinergic medication. In addition, there was a death rate for heavy users of 68%.25 The researchers assumed that the anticholinergics were causing significant stress on body organs and systems. The anticholinergics were also identified as influencing delirium. American studies have substantiated the above. Americans who took an average of three to four anticholinergic medications in a 90-day period were three times more likely to develop cognitive disorders than those patients not taking anticholinergic medications.25 Anticholinergic medications need to be prescribed for the elderly with caution. Not only are doctors often unaware of all the medicines their patients are taking, but the list of drugs with anticholinergic properties is a long one. For instance, of the 36 million Americans over the age of 65, at least 20% are taking an anticholinergic medication. For example, common medications such as the heart drug digoxin, the blood thinner warfarin, the painkiller codeine, and the steroid prednisone are all considered mild anticholinergics. Patients who are taking three or more anticholinergic medications for more than 90 days are over three times more likely to develop mild cognitive impairment. Those with the most severe side effects include Paxil, Benadryl, a drug for overactive bladder called oxybutynin, and the schizophrenia drug clozapine. The clinician should keep in mind that there are many over-the-counter drugs including allergy medications and Tylenol PM whose anticholinergic effects can significantly reduce cognitive function.26

**Lipid-Soluble Medications**

Lipid-soluble medications may also contribute to reduced cognition. Lipid-soluble agents stay in the fatty tissues of the body and slowly enter the bloodstream, resulting in longer periods of sedation. This combined with the depth of the anesthesia and the length of time under anesthesia accounts for what some patients may call the “hangover effect” associated with anesthesia. This hangover effect results in cognitive impairment such as word-finding difficulties and short-term memory loss following surgery. Subsequently, anesthesiologists monitor the length and depth of the anesthesia to avoid these complications.7,9,12

**Cholesterol-Lowering Drugs**

Cholesterol-lowering drugs such as Crestor and Lipitor have been credited with saving the lives of many patients with cardiac disease. However, a small number of recent studies have linked cholesterol-lowering drugs to learning difficulties and memory loss.27 There is concern that the person’s learning difficulties and memory loss could be misdiagnosed as dementia. Other studies have failed to find this link. Current thought is that there may be a small percentage of patients susceptible to cholesterol-lowering drugs. In the susceptible group, it may be just a matter of changing statins.27
CNS Medications

Medications such as benzodiazepines, antipsychotic medications, morphine, and other related pain medications as well as antidepressants including selective serotonin reuptake inhibitors are identified as CNS medications. These medications all affect the nervous system and the brain. Although these medications are useful for the treatment of health difficulties such as anxiety, depression, and pain, they can have a definite negative effect upon cognition. In one study, ~25% of the patients demonstrated cognitive decline, most notably in memory and executive function. Those patients receiving higher dosages of the medications over a longer period of time showed the most declines. Changing the medication to another drug in the same category of CNS drugs may result in a positive change in cognition. Obviously, SLPs cannot change medications. However, the prudent SLP needs to become “best friends” with the agency pharmacist. Every level of health care, from hospital to home care, has a consulting pharmacist who can work with the therapist and make recommendations to the physician.

Medications That May Increase Cognitive Ability

Although many medications are described as decreasing cognitive abilities, there are several that are purported to increase cognitive skills. These medications are thought to alleviate some of the symptoms of cognitive loss in disorders such as AD. These medications, however, do not change the underlying cause.

One medication that has been available since the early 1950s is codergocrine (Hydergine). This medication is not used extensively at this time. There is agreement, however, that this drug can improve self-care and activities of daily living. This medication does not have any specific antidementia effect. It has the effect of elevating mood. It is used as an adjunct to clinical management of mild to moderate cases of AD in the United Kingdom. It is used as part of the clinical treatment of idiopathic mental decline in the United States.

Nootropic agents such as piracetam, oxiracetam, and aniracetam are known as cognitive enhancers. These cognitive enhancers work by increasing brain blood flow, brain metabolism, and oxygen supply to the brain as well as neurotransmitter production in the brain. These agents have been used for several cognitive disorders such as postconcussion syndrome, dyslexia, and dementia. The efficacy of these agents is still open to question.

Nafidrofuryl (Praxilene) is an agent thought to stimulate cerebral blood flow. Efficacy studies have shown a mixed result with this agent for improving cognitive function.

The acetylcholinesterase inhibitors are the most frequently used medications for disorders such as AD to increase cognitive functioning. The physiological activity of acetylcholine has been known since the early 19th century. The neurotransmitter role of acetylcholine has been known since the mid-1920s. It is known that cholinergic degeneration occurs early in AD and that degeneration is associated with cognitive function decline. Several medications have been subsequently developed to inhibit the loss of acetylcholine.

Tacrine (Cognex) was the first agent developed as an acetylcholine inhibitor for AD. Trials of the agent resulted in an approximate 50% dropout rate secondary to adverse side effects. These side effects occurred in 94% of patients. They included vomiting, diarrhea, anorexia, ataxia, flushing, sweating, tremor, and orthostatic hypotension. Many of the side effects resulted in a decrease in oral intake and dysphagia. This acetylcholine inhibitor agent also reported elevated liver enzymes in over 50% of the cases. This elevation in enzymes returned to normal with discontinuation of the medication. This agent has a short half-life of 2 to 3 hours, thus requiring dosage several times daily, and was effective in improving cognition and “setting the time back” to 12 months. Another acetylcholine inhibitor agent is Aricept. This medication received positive efficacy reports for patients described with mild to moderate dementia.

Dropout rates range from 7 to 32%. Negative adverse effects were generally mild and related to vomiting, nausea, diarrhea, fatigue,
and anorexia. Side effects were diminished by starting the medication at a lower dose and titrating over a 6-week period. Aricept has a long half-life of 70 to 80 hours, which allows for daily dosing. Some patients become “emotionally negative” on Aricept, but discontinuation of the medication corrects the problem. Aricept comes in dosages of 5, 10, 15, 20, and 23 mg. The 23-mg dose was introduced just recently and was designed for more severely involved patients. Following the mantra “start low and go slow,” the patient is best started at the 5-mg dose and titrated slowly. Overall it appears that over 40% of patients with Alzheimer’s benefit from this agent cognitively.1,12

A third acetylcholine inhibitor agent is Exelon, which is also available in patch form. This agent is usually dosed twice daily. It is not metabolized by the liver. Drug interactions are very low. This medication was initially developed for people with PD, but it has been utilized with Aricept in some patients where improvement in memory was paramount.1,12

The last acetylcholine inhibitor agent is galantamine (Reminyl). Some studies have indicated improvements for ~ 9 months. This agent was renamed Razadyne due to the familiarity of the original name to another drug. In the same year, the Food and Drug Administration issued a black box warning for this medication. A black box warning is issued to warn the prescriber that use of this medication has been associated with serious side effects and life-threatening risks. Galantamine is not used as frequently as Aricept and Exelon.

Memantine (Namenda) was also introduced as a cognitive enhancer. This medication acts differently from the acetylcholine inhibitors discussed previously. It has a long half-life of 60 to 80 hours. This drug comes in dosages of 5, 10, 15, and 20 mg. Similar to Aricept, the manufacturer states that this medication can be taken by itself, but “does better” in combination with another medication. For this reason, Aricept and Namenda are frequently used together. Titration can occur every 7 days until a daily dose of 20 mg is obtained. Dosages should be lower for patients with renal disease. There have been numerous studies pointing to the positive cognitive effects of this medication. On the other hand, recent studies have begun to question the efficacy of this medication. Side effects include fatigue, hypertension, agitation, drowsiness, confusion, constipation, diarrhea, and urinary incontinence. None of the previously listed medications for cognitive enhancement will achieve total repair of cognitive functioning in the patient. Some studies have pointed to an overall improvement of 10 to 15% in the patient.1

Whether it is medications that result in an increase in cognition or medications that decrease cognition, there are several guidelines that are helpful for the clinician as well as the patient taking the medicine.

- Always ask the doctor to begin with the lowest dose and slowly increase the dose in coordination with the physician’s recommendation. This is particularly true for elderly patients with multiple medications.
- Avoid the use of multiple antipsychotic medications and anticholinergic medications.
- Avoid medications with side effects that exacerbate the patient’s clinical conditions.
- Avoid taking over-the-counter medications without checking with the physician.
- Ensure that the patient has a regular bowel program when taking anticholinergic medications, pain medications, and psychotropic medications.
- Bedside medications should be taken at least 10 minutes before reclining and in an upright position.
- Medications should be taken with adequate amounts of water.
- Medications at risk for esophageal lodging should be taken early in the day and not at bedtime.
- Patients with a history of gastroesophageal reflux disease should be instructed about the foods that may exacerbate the condition.
- The clinician needs to be aware of any changes in cognition with changes in the patient’s medication regimen. These changes need to be reported to the physician.
- The clinician needs to develop a working relationship with both the physician and pharmacist.
SUMMARY

Working with the elderly can be difficult because of their varied physical and cognitive changes and the presence of the polypharmacy challenges. It is essential for clinicians to obtain a clear grasp of these variables if they are to affect meaningful change with their patients. For example, the clinician who does not appreciate the role of medications in cognition can work endlessly without success, because one of the most important variables is not addressed. Because SLPs are not qualified to prescribe medications, a strong working relationship with the consulting pharmacist and physician is essential.

REFERENCES


