Nurses Research Publication
For Continuing Education

Presents:

PHARMACOLOGY UPDATE

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Notice:

Medicine is an ever-changing science. As new information is gained, changes in treatments and drug therapies are required. The author(s), editor, and publisher of this text have used every possible reliable source in order to verify information in this text, to be sure that the information is accurate and the most current and acceptable information available at the time of publication. However, due to human error and/or changes in medical science, neither the editors nor publishers nor any other party involved in the preparation or publication of this text, warrant that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from use of such information. Readers are encouraged to confirm the information contained herein with other sources. For example, and in particular, readers should check the product information sheet for any drugs mentioned in this text that you plan to administer.

This course is designed to provide nursing professionals with general information to assist in their practices and professional development. The information provided in this course is based on research and consultation with medical and nursing authorities, and is, to the best of our knowledge, current and accurate. However, this course is offered with the understanding that Taylor College is not engaged in rendering legal, nursing, or other professional advice. This course is not a substitute for seeking professional advice or conducting individual research. In applying the information provided in this course to individual circumstances, all recommendations must be considered in light of the unique circumstances of each situation. This course book is intended solely for individual use, and not for the benefit of providing advice or recommendations to third parties. Taylor College disclaims any responsibility for any adverse consequences resulting from the failure to seek medical, nursing, or other professional advice, or to conduct independent research. Taylor College further disclaims any responsibility for updating or revising any programs or publications presented, published, distributed or sponsored by Taylor College unless otherwise agreed to as part of an individual purchase contract.

COURSE OBJECTIVES

Long-term Objectives:

1. to help each nurse be informed about the newest drugs in common use

2. to help clients return to optimal health by increasing the level of skill and understanding of the administration of medications in all settings.

3. to help each nurse observe and understand the therapeutic effects and adverse effects of these drugs on each patient

Specific Course Behavioral Objectives:

At the end of this course, each nurse will be able to:

1. score at least 700 on an objective exam on the following:

   *Therapeutic actions, routes of administration, and absorption of drugs *Side effects, adverse actions, and toxic effects of each drug OContraindications and interactions of drugs in each group *Types of drug administration devices used commonly today

2. name and discuss 4 major steps to safely administer an experimental drug.

3. discuss nursing responsibilities with reporting suspected drug abuse among co-workers.

4. discuss the differences between the side effects of drugs and adverse reactions, especially in experimental drugs.

5. discuss the use of infusion pumps and other devices used in hospitals for the administration of IV fluids.

6. discuss insulin infusion pumps used in the hospital and the possible advantages of their use at home.

7. name and discuss at least one drug used for treating AIDS

8. name and discuss at least one new antiarrhythmia drugs listed in the text.

9. name and discuss at least 2 of the new antibiotic drugs mentioned in the text.

CHAPTER I

Introduction to Principles of Pharmacology

Administration of Medications

SELF-EVALUATION:

Each nurse should review the basic principles of administration of drugs before you proceed with this chapter. All information you need to pass the test is contained in this text. However, you may wish to use another reference book to help explain any topics you are not familiar with.

a. the 5 R's
b. pouring the medications
c. charting the medications

The Medication Order .....

The MD will write the order for the drug on the patient chart or on the Emergency Room record. Telephone and verbal orders are acceptable only if the hospital policy allows this. All orders should clearly state the name of drug, dosage, route of administration and the frequency of administration. Be sure that the order is written on the correct patient chart. Most nurses have been taught the 5 R's for the administration of medications. It is true that you should follow these rules, but that is no guarantee that no errors will be made.

Administering drugs .....

In addition to the 5 R's, we wish to **coin the term "Procedural Intuition."** This intuition is that "sixth sense" the nurse has when administering drugs. You may have checked all the 5 R's, but something just does not seem right, so you double check the order. Your "intuition" tells you that someone already gave the drug. You might have noticed that there was a dose of drug missing from the patient's supply. You check again and find out that someone gave the drug and forgot to chart it. Perhaps it was a student or a float nurse or someone else unfamiliar with your procedures.

You must thoroughly know and understand the administration procedure at your facility in order to avoid errors like that just mentioned.

Even if you are one of those nurses who says, "I always double check my meds, out of habit..." That is when mistakes are made. No habit is a good habit. You should always think when you are giving meds; don't do it out of habit. You should administer drugs with the highest awareness, not from habit. Think about every step of the procedure every time you give a drug.

At this point, we surely do not need further lessons in the philosophy of drug administration. The following text will be aimed at a rational and systematic approach to the administration of drugs, and an update on new drugs and new uses for some old drugs. By preventing errors, the nurse will also then have the opportunity to concentrate on possible adverse reactions to drugs and perform patient teaching.

Designing preprinted order forms that prevent medication errors

To minimize communication system errors, one of the steps the ISMP (Institute for Safe Medication Practices) advocates is standardizing communication by using preprinted orders. However, if preprinted orders are not carefully designed and checked, they may actually cause errors. In March 1997, there was a case where a preprinted order listed the dose of magnesium sulfate as 16g **(130mEq), instead of 16 mEg (2cr).** The pharmacist assumed it was correct because it was listed on the preprinted orders. He dispensed the dose. The patient became hypotensive but recovered.

Many healthcare professionals feel a certain amount of comfort with preprinted orders. After all, the orders are usually approved by one or more committees within the institution before they are mass-printed. However, even when the review process is very extensive, errors can slip through or something on the form can contribute to errors. Because preprinted order forms are becoming the standard for many hospital-run protocols, algorithms, critical pathways and guidelines, it is more and more important for institutions to have some methods and rules in place to evaluate and use order forms. We recommend the following when institutions develop preprinted order forms:

Do not use preprinted orders unless all disciplines are involved in the process for developing, reviewing and finally approving the forms

Do not allow orders if they don't coincide with hospital policy (e.g., "renew all previous orders" is not permitted in many hospitals).

Avoid preprinted hospital orders sponsored or prepared by pharmaceutical companies because they may promote a specific product or list non-formulary items. Be sure that blank order forms are accessible only to authorized personnel.

Avoid ambiguous statements such as "unless allergic, give..." because this type of statement transfers clinical and legal responsibility from the prescriber to others down the line. Develop and use a uniform system to indicate orders which should or should not be followed

Use generic names on forms and specify reason for administration when possible. For single source items, brand name should also be included.

Make sure no forbidden abbreviations or dangerous dose designations are used on the forms. Each hospital should have a list of these.

Require the dose per m2 or dose per kg for all chemotherapy and pediatric orders when a calculated dose must be entered.

Do not include a list of drugs to choose from because it's too easy to choose the wrong item (vincristine has been confused with vinblastine)

Force entry of daily dose and number of days for multiple-day regimens.

Express doses by metric weight (e.g., 5 mg) rather than by number of tablets, ml, etc., unless the drug isn't measured by weight (milk of magnesia)

Avoid coined names like "magic mouthwash" or "banana bag" because they may be misunderstood by people unfamiliar with them.

Enhance readability by using fonts and print styles that are of professional quality. Proper spelling and spacing is important (i.e., propranolol -20 mg is easily misread as propranolol 120 mg).

Lines on back copies of any order form are unnecessary and may hide decimal points, or portions of a number or name. Leave them off.

Print a tracking number and revision date on form to ease replacement. Review all preprinted orders every two years or when protocols change.

DRUG ACTIONS

The action of a drug is the specific effect(s) that a drug has upon the body. Many factors influence the action or effects of a drug. One of those factors is the absorption into the body. There are different rates of absorption due to the route of administration. An oral drug will have a slower absorption rate than a parenteral drug and therefore a slower action (in general). In fact, the action can be very different depending upon the rate of absorption. In addition, if the patient has certain medical problems, the rate of absorption can be different.

Factors such as GI problems and circulatory problems can interfere with the absorption and ultimately with the action of the drug. For example, a person with a skin rash and with skin eruptions may not absorb a topical medication at all, if applied to that area. Or, conversely, it may absorb too rapidly in that area. It depends upon the type of lesions present and the type of medication. Also remember that food in the stomach will usually slow down the absorption and affect the action of most any oral drug.

Other factors affecting action of a drug are the distribution and fate of the drug. Distribution refers to the body parts penetrated by the drug after absorption. Some drugs are poorly absorbed by bone tissue, but very easily by skin tissue. This drug would probably be very affective against skin problems but not for bone problems. Distribution can be local, systemic or both. Does the drug cross the blood-brain barrier or the placental barrier?

The fate of the drug refers to the manner in which the drug is detoxified and/or excreted from the body. Some drugs are excreted unchanged from the body via the urine or GI tract. Some drugs are detoxified or changed by the liver or other organs and then excreted from the body. Other drugs are oxidized, or they can break down by themselves and then excreted.

Whichever is the case, the way in which a drug is excreted can affect the action. If a drug such a Chlorpromazine (Thorazine) is ingested by a person with liver disease or hepatic failure, the consequences can be fatal. Thorazine must be detoxified by the liver before it can readily be excreted by the body. Therefore, the nurse should be aware of cases like this one; certain drugs require special consideration as to their fate in the body.

Patient factors must also be considered. Tolerance is one of the biggest factors. Each person has their own tolerance to a specific drug. Tolerance may be natural or acquired through long term drug therapy or abuse. Two similar persons can take a dose of 10 mgm of diazepam (Valium) and it can affect the two persons very differently. One person may have little or no effect from the drug, while the other person may be put to sleep for hours by the effect of the same dosage.

Hypersensitivity should be considered next. Some people, like the one mentioned above, may be hypersensitive to a particular drug. The drug may have the reaction in the patient as if it were a lethal dose. In other words, the person may be overly sensitive to the drug, but the consequences are the same.

Lastly, we will consider the idiosyncratic reaction to a drug. This reaction is a totally unexpected and sometimes "opposite" reaction to a drug. In the broadest definition of the term, a patient may have a totally unexpected violent reaction to a mild drug. This almost sounds like an allergic reaction to a drug, but it is not. An allergic reaction is quite different. The idiosyncratic reaction is completely unexpected and opposite of what is expected. An example is the person who is kept up and restless all night due to the sleeping pill they were given at bedtime. The action can actually be much more violent than the above example.

The nurse must constantly be aware of all possible reactions to drugs. You must also be prepared to handle such problems. You must consider all of these factors before administering drugs. The nurse should always fully understand the patient's diagnosis and have a baseline assessment of the patient, and always ask them if they have taken a medication in the past. This is an invaluable guide for the nurse. If they have uneventfully taken a certain drug in the past, chances are they will tolerate it now. However, if they have never taken a certain drug, the nurse should monitor the patient carefully.

This ends our quick introduction to Pharmacology. If you wish to review any of these topics, you can refer to any basic pharmacology text. The main objectives of this course will center around introducing you to new drugs, or to update you on some of your "old favorites" that are in common use today.

Of course, it is impossible to memorize every drug on the market today. Our objective will be for each nurse to "categorize" drugs and to remember some common side effects of drugs. Each nurse will become more familiar with drugs you use every day.

For example, if you are a cardiac nurse, you will become more familiar with the cardio drugs. However, each nurse should be informed of new drugs and new uses for old drugs, no matter what specialty you are in. Keep these objectives in mind.

We are not trying to test your memory, but rather your "thinking" power:

40,- Be sure you know how to "look up" a drug you do not know.

Be able to "classify" a drug so you will know its general actions and side effects

-WBe sure you can "classify" the side effects of common drugs (not memorize ALL side effects ...it is impossible)
(this will be presented on the following pages)

40o-Be sure you know that some persons may react unexpectedly to some common drugs

40o-Be aware that persons with severe illnesses may not be able to handle the "normal" dosage.

40o-Be aware of factors that can slow or speed up absorption of drugs.

SIDE EFFECTS OF DRUGS

This section is a guide to some of the most common side effects of drugs. It will be much easier to memorize the side effects of a particular drug, if you classify or organize side effects. Remember that this list below is not a complete list. It is well known that a person can have a limitless number of adverse reactions and side effects to drugs. However, this list below is an attempt to show you how to classify side effects to make it easier to study them and remember them.

The following list is divided into systems in order to present common side effects for each system. We have listed these systems in order of priority and severity of side effects. For example, cardiovascular system side effects will tend to be more severe than gastrointestinal side effects. Therefore, we listed them first. A person who experiences hypotension is in more potential danger than a person experiencing nausea. Nausea can certainly be unpleasant, but hypotension could become life-threatening.

Finally, remember to use the following list only as a guide. It is not a complete list of all possible side effects, and it is not to be used as THE ONLY list of side effects that you consult. However, you will find that it is much easier to remember the side effects of a new drug if you group them in logical order.

Example:

You have just looked up a new drug that your patient is now taking: Lisinopril is an antihypertensive drug.

The side effects are:

neutropenia, dizziness, headache, fatigue, depression, somnolence, paresthesia, hypotension, orthostasis, chest pain, nasal congestion, diarrhea, nausea, dyspepsia, impotence, hypokalemia, rash, cough, muscle cramps, angioedema, decreased libido.

If you try to memorize these side effects (above), it is almost impossible. However, classify them, see how much easier it is:

CNS--dizzy, headache, fatigue, depression, paresthesia, lethargy

Cardio--hypotension, orthostasis, chest pain,

GI--diarrhea, nausea, dyspepsia,

GU--decreased libido, impotence, hypokalemia

EENT--nasal congestion, cough

This is one example of how you can classify side effects. When you look up a drug that is new to you, use this as a guide and learn the side effects in a short time. The reference chart is on the next page...

MOST COMMON DRUG SIDE EFFECTS

A Cardiovascular side effects:
hypotension, hypertension, bradycardia, tachycardia, arrhythmia, dizziness, headache, shock **B CNS side effects:**

drowsiness, syncope, vertigo, decreased level of consciousness (LOC), insomnia, nervousness, irritability, or extra pyramidal symptoms (EPS). [EPS are the severe side effects seen with large doses of phenothiazines (Thorazine and others) such as visual disturbances, swollen tongue, tremors, ataxia, posturing, others]
C Gastrointestinal side effects:

abdominal pain, nausea, vomiting, abdominal distension, diarrhea, constipation, changed stools

LESS COMMON SIDE EFFECTS

A Allergic Reaction: urticaria, rashes, anaphylaxis, changes in pulse, symptoms of shock **B Atropine-like side effects:**

dry mouth, blurred vision, flushing, dry skin, tachycardia, urinary retention, constipation, others

LONG-TERM SIDE EFFECTS

A Liver damage: jaundice, petechiae, dark urine, rarely uremia **B Renal Damage:** anuria, oliguria, hematuria, albuminuria, fluid/electrolyte imbalance **C Blood Dyscrasia:**
aplastic anemia, thrombocytopenia, agranulocytosis, leukopenia

Adverse Drug Reactions (Rodinella; Paquet)

within the scope of their practice, nurses administer a wide variety of medications to their patients. However, the nurse's responsibility extends far beyond passing out the correct medication, in the right dose, at the correct time, via the correct route. Virtually all medicines have the capacity to cause adverse effects.

32,000 elderly people suffer hip fractures annually in falls caused by adverse drug reactions. Sixteen thousand car accidents, annually, are attributed to adverse drug reactions.

For marketed drugs in the US, adverse drug reactions (ADRs) account for 3% to 70 of all hospitalizations. In prospective studies, ADRs occurred during loo to 20% of hospitalizations, and to to 200 of the reactions were severe. Nurses have the opportunity to play a key role in identifying, documenting, and even preventing untoward drug reactions.

The Two Extremes

Mr. Johnson, a 56-year-old engineer, seen for back pain in a primary care physician's office, is given a prescription for ibuprofen. He seeks you out after the physician leaves to say, "I can't take this, I'm allergic to Motrin; it gives me a stomach ache." Savvy nurses don't jump to conclusions here. Ibuprofen may still be the drug of choice.

A 15-year-old asthmatic patient who has no known allergies to medications is complaining of a flushed feeling and a lump in his throat after taking a dose of penicillin. The nurse familiar with adverse drug reactions knows that swift action is necessary; the reaction can be fatal.

Allergy Or Drug Interaction? You Decide.

An adverse reaction to a drug is an undesirable and usually unanticipated response that is independent of the therapeutic or diagnostic purpose of the medication. Any reaction that requires a change in the patient's disease management, necessitates a change in dose or discontinuation of the drug or requires supportive treatment, or prolongs the patient's hospital stay can be deemed "adverse." Each year, one to two million Americans has some type of adverse drug experience (ADE).

You may have heard terms used to describe an adverse drug reaction, such as a drug allergy, an idiosyncratic reaction, a paradoxic response, a side effect, or a drug interaction. The term "adverse drug event" encompasses all of these terms. But be aware that each term describes a different **type** of ADE.

There are many schools of thought with regard to classification of adverse drug reactions; within this text, they will be categorized as either immunologic (allergic) or non-immunologic.

Is It A True Drug Allergy?

Allergic reactions to drugs are caused by the interaction between drugs or their metabolites with various effector cells of the immune system. Most drugs or their metabolites are referred to as "haptens" due to their low molecular weight. In order for an allergic response to occur, it is often necessary for the drug or its metabolite to combine with a protein or tissue component in the body. Subsequently, this drug-protein complex, now functioning as an allergen, may stimulate an allergic reaction.

"Antibiotics" is one category of drugs likely to cause allergic reactions; and of these, penicillin or its derivatives is the most frequent culprit.

Penicillin is classified as a beta-lactam antibiotic and is one of the most widely prescribed medications. A hypersensitive reaction to penicillin is not to be taken lightly. Up to l00 of allergic reactions to penicillin are life-threatening.

A mild allergic reaction to penicillin may consist simply of urticaria, which may disappear upon discontinuation of the drug, or upon administration of an oral antihistamine. Be watchful for the potential for cross-sensitivity between penicillins and cephalosporins. If a patient has had an immediate reaction to a penicillin, the potential exists for a similar reaction to cephalosporins and they should usually be avoided.

Vaccines and antitoxins may cause allergic reactions in those individuals who have an egg sensitivity or who have a bovine sensitivity.

Insulin may cause local allergic reactions; erythema, induration, burning, and pruritus at the site of injection. These reactions usually occur within the first one to four weeks of insulin therapy, and almost always disappear in three to four weeks of continued insulin administration. Systemic reactions to insulin are rare.

Anaphylaxis: A Dire Emergency

Anaphylaxis, a potentially severe, systemic adverse response to an antigen or agent is clinically significant because it is potentially fatal and because frequently, there is a missed diagnosis or inaccurate assessment of the severity as a cause of shock of obscure origin.

Factors that may predispose to anaphylaxis are as follows:

- Atopic history -- reactions to ingestants (food or drug) or inhalation agents but no atopic history with injected drugs.
- Length of the interval between exposure or administration and response.
- The shorter the interval, the more likely the response will be severe.
- Consistency of antigen exposure; and/or Route of administration (triggered more often by injection than by oral route).

Urticaria and angioedema are the most commonly seen symptoms (90% of cases) in proven cases of anaphylaxis. Upper airway edema (potentially fatal), asthmatic symptoms, and flushing are each seen in approximately 500 of the cases. Syncope and/or hypotension are seen in about 330 of the cases.

Therefore, if urticaria, angioedema, flushing, or airway obstruction are not present, it is unlikely that anaphylaxis is the cause of shock.

Anaphylaxis may affect the heart directly however, causing arrhythmias. Dysrhythmias, such as sinus tachycardia or ventricular ectopy, may occur. In rare cases, ventricular fibrillation or myocardial infarction may result.

Anaphylaxis is an acute medical emergency requiring **prompt attention.** Delay in treatment can raise the risk of a fatal outcome. The goal of therapy is to maintain the patient's airway, respiratory function, and circulation. Aqueous epinephrine is the mainstay of treatment in anaphylaxis. Depending on the severity of the reaction, other medications such as diphenhydramine (Benadryl), sublingual isoproterenol, inhaled epinephrine, aminophylline, and corticosteroids may be indicated, although none are appropriate as first-line treatment or prevention of anaphylaxis.

When It's Not An Allergy

Nonimmunologic drug reactions may account for greater than 900 of ADEs, and by do not involve allergic or immunologic response. Nonimmunologic drug reactions include side effects, overdoses, drug interactions, idiosyncratic reactions, drug intolerances, and secondary effects.

Side effects refer to the undesirable, yet unavoidable, pharmacologic actions of a drug that occur with predictable low (< 20) frequency and are usually considered clinically acceptable.

Drug interactions involve the alteration of the effects of one drug by the prior or concurrent administration of another drug. For example, thiazides and certain other diuretics when combined with an antidiabetic drug may cause elevated blood glucose levels. The hypoglycemic action of the antidiabetic drug may be counteracted by the diuretic.

Monoamine oxidase (MAO) inhibitors are a family of compounds that are used in treating depression. Patients who have received meperidine (Demerol) while concomitantly receiving an MAO inhibitor, have experienced seizures, hyperpyrexia, severe hypotension or hypertension, respiratory depression, excitation, peripheral vascular collapse, and even death in some cases.

Another example is women who take both phenobarbital and oral contraceptives. Phenobarbital may enhance contraceptive hormone metabolism and minimize contraceptive effects. Alternate birth control methods should be considered.

An individual may simply have a drug intolerance, which implies that there is a lowered threshold in the body to the normal pharmacologic action of the drug. An idiosyncratic reaction may refer to an ADE in which the patient has a genetically determined metabolic or enzyme deficiency, which predisposes her or him to a reaction.

Adverse reactions to aspirin and non-steroidal antiinflammatory drugs (NSAIDS) are usually considered nonimmunologic reactions. However, the mechanism which triggers a response is not well understood. These ADEs tend to trigger symptoms such as urticaria or more severely, bronchospasm, rhinitis, and sinusitis. Bronchospasm induced by aspirin is rare in nonasthmatic individuals; if it does occur, get ready. The reaction may be severe and even life-threatening, especially in the aspirin-sensitive patient with asthma.

Narcotics may cause nonimmunologic reactions, usually those of urticaria or mild hypotension. The resulting mild hypotension usually responds to fluid administration.

It is interesting to note that immunologic and nonimmunologic drug reactions may cause similar symptoms, such as urticaria. Thus, some nonimmunologic drug reactions may be referred to as pseudoallergies, but it is essential that a differential diagnosis be made so that appropriate treatment can be given.

In discussing allergic versus nonimmunologic reactions, it is important to elicit further information when patients describe themselves as allergic to a drug. What may have happened is that they suffered a common side effect, such as nausea due to gastrointestinal intolerance of a drug. In order to rule out an allergic response, a detailed account of events **and symptoms** is required in the history. The person taking the **history plays a vital role in** clarifying the information, in order that, if possible, the drug of choice for treating the patient's condition not be eliminated, and a less-effective drug substituted.

It is very important that you tell your patients what side effects to expect from each of their medications and to encourage them to report unexpected effects. Without this information patients may just stop taking the drug on their own when they encounter any disturbances.

Keeping Tabs On ADEs

All pharmaceutical manufacturers are required to report serious ADEs to the Food and Drug Administration (FDA). The FDA maintains a system to monitor the use of drugs from all pharmaceutical companies in the US to identify potential problems that were not revealed in preapproval clinical studies and in immediately postapproval studies. Reports of serious ADEs may also be referred to the FDA by healthcare professionals, lawyers, and consumers.

In the drug surveillance setting, typically a physician screens the ADE reports that classify the events as mild (do not require antidote therapy or do not prolong hospitalization), moderate (require a change in, but not necessarily cessation of the drug and may prolong hospitalization or require special treatment), or severe.

Severe adverse drug reactions, according to current FDA criteria, are reactions that:

- Result in death
- Are life-threatening (ventricular arrhythmias, shock, massive hemorrhage, anaphylaxis, for example)
- Result in significant or permanent disability
- Require inpatient hospitalization or prolongs a hospital stay
- Result in discontinuation of the drug and treatment for the specific adverse reaction.

In addition, any case where an infant is born with a congenital anomaly to a mother who was on medication during pregnancy is considered serious. Patients who develop cancer while on a medication are also placed in that category.

An unexpected ADE is one that is not listed in the package insert or current labeling for the drug. Expected implies an ADE that is listed in the prescribing information or on the current labeling for the drug. The FDA requires that pharmaceutic manufacturers submit all serious or unexpected ADE reports on their products within 15 working days.

The suspect drug is defined as the drug most likely to be associated with the adverse reactions. It is important to identify the name, dose, frequency, route used, and therapy dates, regarding the product. In some instances, there may be two or more suspect drugs reported as the medications that may have precipitated the event.

Administration of a defective drug or product may also result in an ADE. Examples of product defects include discoloration, change in consistency, evidence of tampering, and incorrect labeling. If you identify a drug as having a potential defect, do not administer it. The product should be returned to the pharmacy, and may be forwarded to the manufacturer for analysis.

In Day-To-Day Practice

Nurses are the eyes and ears for the patient and are therefore usually the first line of defense for ADE monitoring. Nurses employed in any professional capacity indirectly or directly involved in patient care may report reactions. Most institutions, whether acute or long-term care, usually have a specific protocol and procedure for reporting ADEs.

In accordance with guidelines set forth by the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO), hospitals must maintain documentation of adverse drug events occurring during patient hospitalizations. In some cases, these reactions may also be reported directly to the FDA and/or to the pharmaceutical manufacturer.

Typically, the hospital's risk management department reviews the ADEs that occurred in the institution. Further, the hospital's pharmacy and therapeutics committee is also responsible to review adverse drug event reports. JCAHO requires the pharmacy and therapeutics committee to determine if there was in fact an ADE, if it was avoidable, and what, if any, corrective action should be taken. This usually involves what is known as a systems review.

Staff nurses are often the first to identify that a patient has had an adverse drug experience. Of course, the attending physician should be notified when an ADE occurs. You may want to discuss with nursing management how you should handle the documentation or reporting of ADEs in your workplace.

In the past 50 years, remarkable medical advances have been-made, ranging from antibiotics for infectious diseases to drugs for chronic disorders such as arthritis, hypertension, and diabetes. Today, researchers are striving to make further advances in drugs for disorders such as AIDS and Alzheimer's disease. Clinical research attempts to establish what a new drug or compound will do in the human body. However, some of the adverse effects that patients may experience will not become apparent until the drug has been received by many thousands of patients.

In some institutions computer alert systems are being tested to determine their efficacy and efficiency at detecting opportunities to prevent patient injury secondary to a broad range of ADEs.

By identifying and reporting adverse drug experiences, you are helping to continually ensure the safety and efficacy of pharmaceutical products. In the long-run, your efforts support the health and well-being of all patients in the healthcare system and fulfill the primary nursing objective of being the patient's advocate.

The All-Important Drug History:

I. General Information

A. Allergies

1. Drugs (Rx and OTC)
   a. What type of reaction?
   b. What was done to relieve the condition?

2. Food

B. Medical History (Past/Present)

1. Condition

2. Treatments

C. Dietary and Recreational

1. Drug Use

2. Special Diets

3. Use of Alcohol or Tobacco

II. Socioeconomic Status

A. Age

B. Educational Level

C. Occupation

- Document all prior adverse drug events in the history, including the symptoms of the reaction and treatment received.
- Be familiar with the effects; keep in mind other drugs **and foods that** are contraindicated or may change drug efficacy during the drug therapy.
- Observe your patient following administration of medications, especially if they are administered parenterally.

CHAPTER II

Pharmacology Update

ANTIBIOTICS - ANTIINFECTIVES

This is a very large group of drugs. It includes drugs which are used to treat conditions such as bacterial, viral, fungal and parasitic infections. In a normal situation, the body's own defenses come into play in order to fight the infection. However, when the infection becomes too great, the body by itself, cannot eliminate the organism(s). Antibiotics are administered in order to reduce the numbers of organisms to a point where the body can overcome the infection. Most antibiotics are very selective about the organisms on which they will act. Narrow spectrum antibiotics treat the most limited types of organisms. Broad spectrum antibiotics treat a "broader" range of organisms.

Antibiotics or antimicrobial agents, are derived from cultures of a microorganism or produced semi synthetically, and are used to treat infections. The penicillins, derived from species of the fungus penicillium or manufactured semi synthetically, consist of a thiazolidine ring fused to a beta-lactam ring connected to side chains; these agents exert their action by inhibiting mucopeptide synthesis in bacterial cell walls during multiplication of the organisms. Penicillin G and V are widely used in treating many gram-positive coccal infections but are inactivated by the enzyme penicillinase produced by strains of staphylococci; cloxacillin, dicloxacillin, methicillin, nafcillin, and oxacillin are penicillinase-resistant penicillins.

When an antibiotic agent is prescribed, many factors must be considered by the physician. First, the patient's general condition is assessed. Some antibiotics are very toxic to select body systems and the MD must be sure that the patient can tolerate the antibiotic. Next, the organism must be identified. A culture is obtained and the proper antibiotic sensitivity is determined. Next, the site of the infection is considered. Some antibiotics work better parenterally than topically, for example, so the site of the infection must be considered, as well as other factors.

The ANTIBIOTICS/ANTIINFECTIVES may be divided into many different categories. The "Nursing 2000 Drug Handbook" from Springhouse Corp., divides the drugs into the following very logical categories. These are certainly not the only way to classify the antibiotic drugs. There are many ways in which to study these drugs.

However, classifying these drugs according to their actions and uses, seems to be the best method:

SAmebicides and antiprotozoals
OAnthelmintic
eAntifungals
OAntimalarials
*Antituberculars and antileprotics
SAminoglycosides
*Miscellaneous Antiinfectives
OPenicillins
eCephalosporins
*Tetracyclines
eSulfonamides
OQuinolones
OAntivirals
*Oxazolidiones

COMPLICATIONS OF ANTIBIOTIC THERAPY

ANAPHYLAXIS--

-Antigen-Antibody Reaction
-Histamine released from Mast Cells
-Dilation of small blood vessels (flushing)
-Bronshoconstriction
-Stimulates salivary glands
-increases catecholamines by adrenals

Treatment:

-Epinephrine 1:1000, initial dose 0.3 to 0.5 ml subQ every 20 min to 4 hours
-Benadryl, adjunctive to epinephrine (initial dose 10-50 mg IV or deep IM)
-IV Fluids
-Corticosteriods; (Decadron 10-100mg, Solucortef 1000mg, or Solumedrol 1000mg
-Supportive therapy; maintain airway, etc.

Antibiotics and the Elderly Patient:

The health care team must consider a wide variety of factors when the elderly person is to be started on antibiotics therapy. The aging process causes a number of physiological changes in the body that could alter the effects of drugs on the body. Absorption of drugs from the gastrointestinal tract is altered. There is reduced blood flow to the gastrointestinal (GI) tract, gastric pH is elevated, and gastric emptying is usually delayed in the elderly. Therefore, there is a potential for variability of absorption of drugs in the elderly. In fact, the elderly are susceptible to ototoxicity and to nephrotoxicity when taking aminoglycoside drugs such as gentamicin, tobramycin, amikacin, and streptomycin. They seem to be at increased risk, due to the decreased creatinine clearance with age.

There is also a problem that the elderly seem to have with taking multiple drugs. There can be drug-drug interactions between these drugs that the elderly may be taking. The classical example of this is the elderly person who takes antacids and there is interference with tetracycline absorption. The elderly may have changes in absorption when a drug is administered IM, due to altered peripheral circulation. Altered blood flow might also affect the distribution and the metabolism of antibiotics and other drugs that the elderly might take. This topic is discussed in detail later in this workbook. Medication-related injuries are on the increase in the elderly. Problems include, but are not limited to, multiple medications, over-dosing, and drug interactions. Nurses in all areas of practice must be aware of these problems and act as an advocate for the elderly.

In summary, the treatment of all patients with antibiotics will depend upon many factors. If all factors are not considered carefully, the patient may not be treated adequately and in some cases, be harmed by the treatment.

New antibiotic combats drug-resistant infections: (Ford)

Linezolid (Zyvox) is the first antibiotic in a NEW CLASS of antibiotics approved by the FDA to combat the problem of drug-resistant infections attributed to *Enterococcus* and *Streptococcus. Zyvox* was brought to market in April 2000, a member of a new class called the *oxazolidinones.* Drugs in this class are active against Gram-positive bacteria. The new drug will be used primarily in the inpatient setting or in nursing homes, where patients are most at risk for serious, drug-resistant infections such as; E. faecium, S. aureus, S. pneumoniae, and S. agalactiae. Keep in mind that this drug is used only with certain strains of these organisms and only when these strains prove to be resistant to other antibiotics.'

Zyvox acts by inhibiting bacterial protein synthesis at a unique point in the bacteria life-cycle. Zyvox also offers 100. bioavailability. This means that blood levels achieved after oral administration of the drug are the same as those obtained with intravenous use. This fact has numerous benefits including that the patient may be discharged from the hospital while ensuring that he receives the same dose of the drug at home as he received in the hospital.

The most common side effects are headache, nausea, diarrhea, vomiting, insomnia, and constipation. Thrombocytopenia may occur, requiring the monitoring of the patient's platelet counts. Zyvox may interact with pseudoephedrine and phenylpropanolamine2 (PPA), causing an elevated blood pressure. Zyvox may inhibit monoamine oxidase, so patients receiving this drug must avoid foods with high tyramine content (same diet as patients taking MAO inhibitor drugs).

More Antibiotic Updates

FLUCYTOSINE (5-FC), Ancobon, Antifungal drug

*Indications: severe fungal infections caused by Candida; Cryptococcus infections
*Side Effects: nausea, vomiting, dizziness, headache, vertigo, diarrhea, confusion, rash, anemia
050-150 mg/kg daily; drug is usually combined with amphotericin; monitor I&0; blood levels should be monitored for therapeutic dose of drug and for resistance to drug.

Including Vancomycin, which up to now, has been the last line of defense for certain infections.

Interaction with PPA may no longer be a problem as the FDA has recommended withdrawal of PPA from the U.S. market. However, there may still be products with PPA in them. Be sure to take a complete patient drug history.

LORACARBEF, Lorabid, Eli Lilly, Broad-Spectrum oral Antibiotic

*Indications: mild to moderate respiratory infections, skin and urinary tract infections
*Side Effects: nausea & vomiting, diarrhea, headache
0200mg-400mg TID to QID; very few side effects or adverse effects reported, generally well-tolerated

MOXALACTAM, Moxam, Third-generation Cephalosporin Antibiotic

*Indications: serious respiratory infections; serious urinary tract infections, intra-abdominal infections; septicemia; E. coli infections; pseudomonas; peptostreptococcus infections, many others
OSide Effects: nausea & vomiting, diarrhea, anorexia, thrush, headache, dizziness, malaise, rashes, urticaria

02-6 G., IM or IV daily in divided doses, 5-10 day therapy;

This drug is very well tolerated. Today, this drug is being used for the very serious infections that don't respond to traditional antibiotic therapy. The usual side effects of the cephalosporins are seen with this drug. However, most people have very few serious adverse effects. Nursing considerations will include observing for the LONG-TERM EFFECTS OF drugs in this group. These long-term effects include: neutropenia, eosinophilia, hemolytic anemia, hypoprothrombinemia, bleeding.

MISCELLANEOUS: ANTIBIOTICS - ANTIINFECTIVES

Sporanox (itraconazole capsules) Janssen

Sporanox is indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:

1. Blastomycosis, pulmonary and extrapulmonary
2. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis
3. Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy
4. Onychomycosis due to dermatophytes (tinea unguium) of the toenail with or without fingernail involvement

Side Effects: Side effects include constipation, gastritis, depression, insomnia, tinnitus, menstrual disorder, adrenal insufficiency, gynecomastia, and male breast pain.

CEFEPIME HCL New-generation cephalosporin

Cefepime (Maxipime, Bristol-Myers Squibb) has been designated by many as the first "fourth-generation" cephalosporin. It's highly active against many bacteria, including some organisms that have become increasingly resistant to other cephalosporins.

Although the third-generation cephalosporins are highly active against many gram-negative bacteria, some exhibit only weak activity against gram-positive bacteria (for example, Streptococcus pneumoniae). Cefepime, however, demonstrates greater activity than most of the third-generation drugs against gram-positive cocci. Cefepime is as active or more active against most gram-negative bacteria than the parenterally administered third-generation cephalosporins. Cefepime is indicated to treat patients with moderate to severe pneumonia, urinary tract infections, and uncomplicated skin and skin structure infections caused by susceptible bacteria.

Precautions:

(1) Cefepime is contraindicated in patients who have had immediate hypersensitivity reactions to a cephalosporin, penicillin, or other beta-lactam antibiotics.
(2) Up to 100 of patients with a history of penicillin allergy demonstrate cross-hypersensitivity to cephalosporins. Exercise extreme caution if it's necessary to administer cefepime to a penicillin-sensitive patient.
(3) Don't mix solutions of cefepime with solutions of metronidazole, vancomycin, gentamicin, tobramycin, or netilmicin because of possible incompatibility. If concurrent therapy is indicated, administer the antibiotics separately.
(4) Patients with impaired renal function or those undergoing hemodialysis require dosage adjustment; consult the product labeling.
(5) A decrease in prothrombin activity has been reported in some patients taking cefepime. Monitor prothrombin times in patients at risk (for example, patients with renal or hepatic impairment or poor nutritional status) and administer vitamin K as indicated.
(6) Use cefepime with caution in patients with a history of gastrointestinal disease, particularly colitis. Cefepime may cause colitis (including pseudomembranous colitis).

MEROPENEM, Broad-spectrum antibiotic

Meropenem (Merrem I.V., Zeneca) is the second carbapenem antibiotic to be marketed in the United States, joining imipenem (which is coadministered with cilastatin [Primaxin]). Like its predecessor, meropenem is administered parenterally and has a broad spectrum of action that includes many gram-negative and gram-positive bacteria, including some that are often resistant to other antibiotics.

Meropenem has been initially approved for only two indications:

- adult and pediatric patients with intra-abdominal infections (complicated appendicitis and peritonitis)

- pediatric patients (3 months of age and older) with bacterial meningitis caused by susceptible strains of bacteria.

*Because of its broad spectrum of activity, it's useful as first-line, single-drug therapy before the causative organisms are identified.

Precautions:

(1) Meropenem is contraindicated in patients with known hypersensitivity to imipenem and in those who've had anaphylactic reactions to penicillins, cephalosporins, or carbacephems. Avoid using meropenem even in patients who've had less serious hypersensitivity reactions to these antibiotics. If meropenem is indicated, closely monitor the patient's response.
(2) Don't mix meropenem with or add it to solutions **containing other drugs.** (3) Carefully monitor treatment in patients at risk for seizures.
(4) Consult the product labeling for dosage recommendations for patients with creatinine clearance of less than 51 ml/minute.
(5) Don't give concurrently with probenecid (Benemid), which inhibits the tubular secretion of meropenem, increasing its serum concentration and activity.

Adverse reactions: diarrhea, nausea/vomiting, headache, inflammation at the injection site, rash, pruritus, oral moniliasis, **seizures**

Fluoroqiunolones Update:

In the past ten years, quinolones have become an important, expanding group of antimicrobial agents. The first quinolone nalidixic acid (NegGram) manufactured by Sanofi Pharmaceuticals was approved by the Federal Food and Drug Administration (FDA) for clinical use in the United States in 1963. Poor serum levels combined with the rapid development of bacterial resistance relegated nalidixic to a minor role in the treatment of urinary tract infections. The addition of a fluorine group and a piperazine substituent greatly enlarged the effective antibacterial spectrum of quinolones. The addition of a methyl group on the piperazine ring further enhanced the bioavailability of the quinolones.

Norfloxacin and ciprofloxacin were the first two fluoroquinolones released for clinical use in the United States. They now have been joined by several other fluoroquinolones including the four drugs that will be discussed in this course: levofloxacin, sparfloxacin, grepafloxacin and trovafloxacin.

General Properties of Fluoroquinolones:

The fluoroquinolones are bactericidal, broad-spectrum antimicrobials that act mainly by blocking DNA gyrase; a bacterial enzyme that maintains the super twisted helical structure of DNA. The following organisms are very sensitive to these quinolones: Enteric gram-negative bacilli including: E. Coli, Proteus, Klebsiella, and Enterobacter; common gastrointestinal pathogens including: Salmonella, Shigella, and Campylobacter.

Other gram-negative organisms include:
N. gonorrhea, N meningitides, H influenzae, Pasteurella multocida, M. catarrhalis, and Yersinia enterocolitica

Other organisms affected to a lesser degree are:
P. aeruganosa, Acinetobacter, Serratia and Staphylococci (S, aureus, and S. epidemidis) and streptococci (including pneumococci, and enterococci)

Some intracellular pathogens are inhibited by some quinolones:
Chlamydia, Mycoplasma, Listeria, Legionella, and M. tuberculosis.

These drugs are well tolerated with mild gastrointestinal side effects (nausea, vomiting, or anorexia) and central nervous system (CNS) side effects (light -headiness, dizziness, somnolence or insomnia) that effect less than 10% of treated patients. Joint problems have been reported, specifically tendinitis which has resulted in rupture of the shoulder, hand and Achilles tendons.

Exposure to direct sunlight has resulted in moderate to severe phototoxicity reactions in patients when taking drugs of this class. Therefore, direct exposure to sunlight should be avoided.

LEVOFLOXACIN

The fluoroquinolone antibiotic levofloxacin (Levaquin) received FDA approval December 20, 1996 for respiratory, skin, and upper and lower urinary tract infections. In addition, it is more effective against gram-positive organisms and anaerobic organisms than former quinolones.

It also is the first once-a-day antibiotic proven effective against three of the most difficult to treat bacterial respiratory infections: community-acquired pneumonia, acute maxillary sinusitis, and acute exacerbation of chronic bronchitis which collectively affect more than 50 million people each year.

Levofloxacin (Levaquin) is the active 1-isomer of ortho's quinolone of loxacin (Floxin). This isomer has an improved tolerability, longer duration of action and is more effective than ofloxacin (Floxin) and other quinolones against bacteria. Like other quinolones, levofloxacin inhibits bacterial DNA gyrase and prevents DNA replication, transcription, repair and recombination in susceptible bacteria.

Indications and Usage: Levofloxacin is indicated for treatment of mild, moderate and severe infections caused by susceptible microorganisms in ADULTS 18 years and older. Prior to the administration of any fluoroquinolone including levofloxacin, sparfloxacin, grepafloxacin and trovafloxacin, appropriate culture and sensitivity tests should be done to determine the susceptibility of the infection causing organisms. However, treatment can commence before the results of these tests are obtained and therapy can be adjusted when the findings are known. Some strains of Pseudomonas aeruginosa may become resistant to levofloxacin fairly rapidly, as it does with other drugs in this class. Therefore, it is advisable to conduct sensitivity tests during therapy to determine the susceptibility and resistance of the organisms to the antimicrobial in use.

General Precautions, Adverse Reactions, and Contraindications:

Serious and rarely fatal hypersensitivity and/or anaphylactic reactions have been reported in patients receiving quinolone therapy, usually occurring after the first dose. Therefore, levofloxacin should not be given to any patient that has had a sensitivity to any of the quinolones or any components of levofloxacin and the drug should be immediately discontinued with the first appearance of a skin rash or any sign of drug sensitivity. Some of the reactions that can occur with hypersensitive patients following the first dose of levofloxacin are: Cardiovascular collapse, hypotension, seizure, loss of consciousness, convulsions, toxic psychosis, increased intracranial pressure, central nervous system stimulation, tremors, restlessness, anxiety, lightheadedness, confusion, hallucinations, depression, nightmares, paranoia, depression, and rare suicide thoughts or acts. If any of these symptoms occur, the drug should be discontinued immediately.

Drug Interactions:

There is up to 98o decreased absorption of levofloxacin when the following drugs are given simultaneously with levofloxacin. oral doses of levofloxacin should be administered at least two hours before or two hours after ingestion of antacids containing aluminum, magnesium or calcium; sucralfate; iron preparations; and multivitamin/mineral supplements containing zinc or other multivalent cations. If the patient is taking NSAIDs, there may be increased CNS stimulation. If increased CNS stimulation occurs, monitor the patient for seizure activity. Warfarin and derivatives tend to have increased levels with some fluoroquinolones. In these cases, the PT and INR should be monitored. Theophylline clearance is decreased with some fluoroquinolones. In this case, theophylline levels should be monitored. Azlocillin, cimetidine, and probenecid increase quinolone levels.

Levofloxacin may cause abnormal Electrocardiogram (ECG) readings, decreased lymphocyte count and it also may cause hypoglycemia or hyperglycemia in patients taking levofloxacin and antidiabetic agents concomitantly.

SPARFLOXACIN

The fluoroquinolone antibiotic Sparfloxacin (Zagam) received FDA approval in the United States December 19, 1996. Sparfloxacin is a long-acting, broad-spectrum, and well-tolerated antimicrobial available in 200 mg tablets only. Like levofloxacin, sparfloxacin inhibits DNA gyrase preventing replication, repair and recombination in susceptible bacteria.

Indications and Usage:

Sparfloxacin, as with levofloxacin should be used for ADULTS 18 years and older and the safety and efficacy of sparfloxacin in adolescents (under 18 years of age), pregnant women and nursing women has not been established. Before the administration of sparfloxacin, culture and sensitivity tests should be done and, sparfloxacin can be administered prior to the results of the culture and sensitivity tests. Dosage: 400 mg on day 1, then 200 mg daily for 9 days (11 tablets total).

Sparfloxacin is contraindicated in patients with pro-arrhythmic conditions such as: hypokalemia, significant bradycardia, congestive heart failure, myocardial ischemia, and atrial fibrillation. Similar to levofloxacin, patients receiving sparfloxacin that are known or suspected of having any CNS disorders such as epilepsy or are predisposed to seizures should be monitored carefully.

Patient Advise:

Avoid exposure to all sunlight, direct, indirect, diffused, cloudy weather or with sunblock use and exposure to ultraviolet light during treatment with sparfloxacin and for 5 days after treatment ceases.

Discontinue sparfloxacin therapy and notify your doctor at the first sign of phototoxicity reaction such as: itching, burning sensation, redness, swelling, blisters, rash, or dermatitis. The patient should avoid exposure to sunlight or ultraviolet light until the phototoxicity reaction has ceased and she/he has completely recovered from the reaction or for 5 days which ever time period is longer. In rare cases, phototoxicity reactions have lasted several weeks after stopping sparfloxacin.

Drug Interactions:

- Methylxanthines: Sparfloxacin does not increase plasma theophylline concentra tions.
- Warfarin: Sparfloxacin does not increase the anticoagulant effect of warfarin.
- Probenecid: The pharmacokinetics of sparfloxacin is not affected by probenecid.
- Digoxin: Sparfloxacin has no effect on digoxin.
- Cimetidine:Cimetidine doesn't effect the pharmacokinetics of sparfloxacin.
- Antacids and sucralfate: Aluminum and magnesium cations in antacids and sucralfate form chelation complexes with sparfloxacin. The bioavailability of sparfloxacin is reduced unless there isat least a four hour wait after sparfloxacin administration before these antacids or sucralfate is taken.
- Zinc and Iron Salts: should be taken 4 hours after sparfloxacin administration, becausethe bioavailability of sparfloxacin is reduced if taken sooner.

Laboratory Test Interactions:

False-negative culture findings can result for Mycobacterium tuberculosis due to suppression of mycobacterial growth during sparfloxacin therapy.

GREPAFLOXACIN

The fluoroquinolone antibiotic Grepafloxacin (Raxar tablets), manufactured by Glaxo Wellcome received FDA approval, November 6, 1997. It is a wide-spectrum once-daily antimicrobial with an improved activity against Gram-positive organisms, especially Streptococcus pneumoniae. As with other quinolones, Grepafloxacin inhibits bacterial DNA gyrase, which is needed for duplication, transcription and repair of bacterial DNA.

Indications and Usage as with other fluoroquinolones, grepafloxacin is indicated for the treatment of ADULTS over 18 years of age. The safety and efficacy of grepafloxacin for adolescents under 18, pregnant women, and nursing women has not been established and carries an FDA Pregnancy Risk Category of "C." It should be noted that, as with other quinolones, culture and sensitivity tests should be done prior to the administration of grepafloxacin to determine the sensitivity of the infecting organism to grepafloxacin. However, treatment can be started immediately and treatment adjusted if necessary when test results are known.

Grepafloxacin (as with other fluoroquinolones) should be used with caution in patients with known or suspected CNS disorders such as severe cerebral arteriosclerosis, epilepsy, and other conditions **predisposed to** seizures.

Tendon ruptures that required surgical repair have been reported in patients receiving quinolones. Grepafloxacin should be discontinued if the patient experiences pain, inflammation or rupture of a tendon.

TROVAFLOXACIN

Oral and intravenous formulations of the fluoroquinolone antibiotic trovafloxacin (Trovan) manufactured by Pfizer were approved by the FDA December 18, 1997. Trovafloxacin was approved for use against 14 bacterial infections, the largest number of indications ever included in an initial drug approval in the United States. Trovafloxacin is effective against gram-positive, gram-negative, atypical, and anaerobic bacteria. Trovafloxacin is also the first agent ever approved for oral prophylactic use in surgery. More than 13,000 patients participated in 87 studies and 30 comparative clinical trials.

Antibiotic Update; Case Studies (Clark)

***These case studies are from the point of the physician, but the nursing considerations of these drugs are also discussed.**

Question: Tally Bing is a 4th year medical student who has just started his elective in Emergency Medicine and you have him on your Saturday morning shift. He has already examined a patient while you were getting coffee and putting on your scrubs.

His first patient is a 23 year old female with pharyngitis who was seen at another hospital 3 days ago and placed on a prescription of cephalexin. She is no better and has not taken her medication because she didn't have the money to fill the prescription. What are the most common barriers to a patient actually taking her antibiotic prescription?

Answer: Factors that keep patients from being compliant are:

1. Taking medication more than 3 times a day. 2. Taking it more than 5 days in a row. 3. Taking it if the medication makes them feel worse. 4. Medication cost of more than 15 dollars.

Since the patient is not allergic to penicillin you suggest your student order an injection of benzathine penicillin to insure compliance. The dose, you tell him is 1.2 million units for patients weighing over 27 kg and 600,000 units for patients weighing under 27 kg.

Question: Bing asks you what are your criteria for diagnosing strep pharyngitis, absent the results of a strep culture or strep antigen.

Answer: According to one authority, patients presenting with pharyngitis and all of the following should be treated for presumed Group A Beta Hemolytic Strep (GABHS):

1. Fever over 38.3 centigrade
2. Pharyngeal or tonsillar exudates
3. Tender anterior cervical adenopathy

An alternative oral regimen is Pen V 500 mg TWICE A DAY for 10 days. However, the patient must take the medication for a full ten days to insure eradication of the GABHS.

Question: Bing has used many of the available fourth generation fluoroquinolones in his medical school for many infections on the medical and surgical wards. He wonders if that class- of drugs is used a lot in your hospital?

Answer: You tell him that you limit the use of these agents, primarily because of the danger of resistant organisms. You remind him that resistance to fluoroquinolones is transmitted by a single plasmid, which confers resistance to the entire class of agents. Major resistance may be rapidly spread with their indiscriminate use.

Question: And what about drug resistant S. Pneumoniae (DRSP)? Is this a problem in your hospital as well?

Answer: There is much concern over the emergence of DRSP. S. pneumoniae is the major pathogen implicated in respiratory tract infections and meningitis. In vitro penicillin resistance exists among 10-300 of pneumococcal isolates. Risk factors for this phenomenon are young age, recent use of antibiotics, day care attendance, and hospitalizations.

Indeed there are sufficiently convincing case reports of pneumococcal meningitis related to resistant isolates that have failed to respond to third-generation cephalosporins. In these cases many experts now recommend that initial empiric treatment of bacterial meningitis should include the addition of vancomycin to a third-generation cephalosporin.

Question: "But vancomycin can't be used for all cases of DRSP," Tally Bing remarks. Isn't there another alternative?

Answer: Several new fluoroquinolones have been or soon will be introduced with respiratory tract infection indications and extended in vitro activity against resistant gram-positive bacteria, including penicillin-resistant S pneumoniae and other DRSP.

You remind him that the fluoroquinolones are representative of the fourth generation quinolones. The first generation quinolone was nalidixic acid (you remember that from your medical school days), the second was norfloxacin and the third, of course, was ciprofloxin.

Question: What other resistance patterns are presently emerging?

Answer: Over the past 5 years in the United States, resistance of outpatient E coli urinary isolates to TMP/SMX has risen to approximately 200, with rates as high as 50% in certain centers.

Question: Your next patient of the morning is a 52 year old diabetic female who was sent to the ER by her family doctor because of a urine culture positive for pseudomonas that is only.sensitive to aminoglycosides. She appears to be clinically nontoxic - you recommend admission to your new ER observation unit and order a creatinine and chemistry panel. What dose of an aminoglycoside such as gentamicin is appropriate if her renal function is normal? Is the creatinine is elevated?

Answer: Single daily dosing of gentamicin is recommended because it has been shown to reduce renal toxicity. The dose is 5 mg/kg/24 hrs (single dose - rounded to the nearest 10 mg). Such dosing is not recommended in children or in patients with liver failure, cystic fibrosis, endocarditis, pregnancy, burns, tuberculosis, neutropenia, or severe renal failure with <20 ml/min creatinine clearance.

If renal failure is not severe, dosing is remembered by one of these two methods:

a. The dose interval can be extended by an amount equal to the initial interval (24) multiplied by the serum creatinine, or

b. Reduce the total daily dose by an amount equal to the initial dose divided by the serum creatinine.

Quinupristin and dalfopristin

Delivering a one-two punch to vancomycin-resistant bacteria approved under the Food and Drug Administration's (FDA's) accelerated approval protocol, quinupristin and dalfopristin (Synercid, Aventis Pharma) are the first drugs in a new class of antibacterial drugs called streptogramins to be marketed in the United States. The two drugs, available only in combination and administered intravenously (I.V.), represent an important advance against life-threatening vancomycin-resistant Enterococcus faecium (VREF) bacteremia. The drugs aren't effective against E. faecalis. The combination product is also approved for treatment of complicated skin and skin structure infections caused by methicillin-susceptible Staphylococcus aureus and Streptococcus pyogenes. However, because of the potential for more severe adverse effects, these infections should be treated with the new drugs only when they fail to respond to conventional regimens.

In clinical trials, the most common sites of VREF infection were intra-abdominal, skin, and urinary tract, but in many patients, no specific site was identified. Many patients experienced clearance of VREF bacteremia within the first 48 to 72 hours of therapy. Most patients experienced inflammation and pain at the peripheral I.V. infusion site; in some patients venous adverse reactions were severe enough to halt therapy. Administering the drug via a central line minimizes these problems.

Precautions: (1) Contraindicated in patients with known hypersensitivity to quinupristin or dalfopristin. (2) Because of the potential for arrhythmias, avoid using concurrently with drugs such as cisapride (Propulsid) that may prolong the QT interval and are metabolized via the CYP3A4 pathway. The quinupristin/dalfopristin combination inhibits this pathway. (3) In patients also being treated with cyclosporine (Neoral), which is also metabolized via the CYP3A4 pathway, closely monitor serum cyclosporine concentrations. See the product insert for a complete listing of precautions related to other drugs metabolized via this pathway. (4) Because quinupristin/dalfopristin inhibit bacteria that help metabolize digoxin in some patients, monitor for elevated serum digoxin concentrations in patients receiving these drugs concurrently. (5) A reduction in the dosage of quinupristin/dalfopristin may be indicated in patients with impaired hepatic function.

Adverse reactions: inflammation, pain, and edema at the infusion site; nausea; vomiting; diarrhea; rash; arthralgia and myalgia; abnormalities in total and conjugated bilirubin levels

CARDIOVASCULAR DRUGS UPDATE

One of the newest classifications of drugs to appear is the calcium antagonist group. Also called the calcium channel blockers, this group of drugs is now in very widespread use in treatment of coronary heart disease and many other cardiovascular conditions, including arrhythmias. The drugs in this large group, though having many different chemical structures, all have the same basic action. Although this group of drugs in not new, many of the uses and indications are new. There are always new forms of this drug classification springing up. There is still much research going on with the drugs in this classification.

They inhibit calcium flux across the cell membrane. The exact effect of the drug will depend upon several factors. Among these is the specific cardiac cell which is involved and the extent of use of calcium by that particular type of cell.

1. Procardia, nifedipine, is primarily used for vasospastic angina. It dilates the coronary arteries, inhibits coronary artery spasm and reduces the oxygen consumption.

Nursing Implications ....

a. dose: 10-30mg PO Q4-Q8h / l0mg SL
b. headache, hypotension, flushing, pedal edema, dysesthesias

2. Verapamil (Calan, Isoptin), another calcium antagonist, is used for slowing arrhythmias such as atrial flutter or fibrillation or supraventricular tachycardia. Recently, it has been used for angina.

3. Cardizem (diltiazem), a calcium antagonist; this drug dilates the coronary arteries and, like Procardia, reduces arterial spasm and reduces oxygen consumption by the myocardium.

a. contraindicated in those with 2nd or 3rd degree AV Block
b. should not be used concurrently with Digoxin or beta blockers
c. contraindicated in liver disease (metabolized in the liver)
d. dosage: 60-90mg PO Q8 hours or 75 to 150 mcg/kg IV

Emergency Drug TheraT)y

Most Frequently Encountered Drugs

Epinephrine is a catecholamine that increases heart rate, myocardial contractility, vascular resistance, and automaticity of the heart. Providers directing code teams prescribe this agent for patients sustaining ventricular fibrillation; pulseless ventricular tachycardia; asystole; and pulseless electrical activity (PEA), formerly known as electromechanical dissociation (EMD). The usual dose of epinephrine is 1 mg IV push (IVP) with repeated doses every three to five minutes according to patient response. Epinephrine is most commonly supplied on code carts in prefilled 10 cc syringes (10 cc = 1 mg, if a 1:10,000 dilution is used). A new AHA guideline recommends the use of a continuous infusion of epinephrine (2 mg/min to 10 mg/min) in symptomatic bradycardia after atropine, transcutaneous pacing, and dopamine has been tried (but before isoproterenol).

The AHA has also provided regimens for the administration of higher doses of epinephrine if there is no response to the initial 1 mg dose. Higher dose epinephrine may be divided into three categories: intermediate doses of 2 mg to 5 mg IVP every three to five minutes, escalating doses of 1 mg to 3 mg to 5 mg IVP three minutes apart, or a high-dose range of 0.1 mg/kg IVP every three to five minutes. At the present time, the efficacy of higher doses of epinephrine is uncertain.

Atropine is used to treat patients with symptomatic bradycardia, atrioventricular (AV) blocks, and asystole. It is also given to patients in PEA, after epinephrine and other therapeutic modalities have failed.

Atropine is an anticholinergic drug that has a direct vagolytic effect. By stimulating SA node automaticity and AV conduction, this agent augments heart rate, systemic vascular resistance, and blood pressure. For asystole give 1 mg IVP every three to five minutes up to a maximum of 0.04 mg/kg. In symptomatic bradycardia the dose is 0.5 mg to 1 mg IVP, repeated every three to five minutes as needed up to 0.04 mg/kg. Atropine is most commonly supplied in pre-filled syringes with 1 mg in 10 cc.

When administering atropine, remember the following points. First, your patient's pupils will become dilated; therefore, pupil checks have no clinical significance. Second, because atropine may produce tachycardia, exercise caution with patients whose electrocardiograms (EKGs) reveal acute changes of ischemia or injury due to increased oxygen demand. Third, atropine is contraindicated in patients who have received heart transplants. When this **procedure is performed, the vagus nerve** is severed and atropine will not be effective. Finally, watch for side effects like tachyarrhythmias, delirium, flushed skin, ataxia, blurred vision, and coma.

Lidocaine, a treatment for ventricular fibrillation (after epinephrine), ventricular tachycardia, and wide-complex tachycardias of unknown origin, is the most commonly used ventricular antiarrhythmic. Lidocaine suppresses automaticity of the HIS-Purkinjie system and elevates the electrical stimulation threshold during diastole. A therapeutic effect reduces ventricular ectopy and enhances response to electrical countershock.

The usual dose for ventricular fibrillation is 1.0 mg/kg to 1.5 mg/kg IVP every three to five minutes to a maximum of 3 mg/kg. The dose for ventricular tachycardia is 1 mg/kg to 1.5 mg/kg IVP with doses of 0.5-0.75 mg/kg repeated up to a maximum dose of 3 mg/kg. Following the lidocaine bolus, institute a continuous IV infusion (2 gm/500 cc D5W) at 2 mg/minute to 4 mg/minute.

Prophylactic lidocaine with acute myocardial infarction is no longer recommended: Reserve a drip for serious, documented ventricular ectopic event.

Administer this drug with caution in patients with conduction disturbances, avoiding it all together for patients in third-degree heart block with ventricular escape patterns. Large doses may depress the sinus node and produce heart blocks. Also, you might want to reduce the dosage for those who have impaired hepatic function, pulmonary edema, and shock or who are over the age of 70. Be alert for signs and symptoms of toxicity, which may include drowsiness, disorientation, tinnitus, paresthesias, and seizures. If toxicity is suspected, stop the drip, hang a normal saline IV, and promptly notify the physician.

Adenosine is a relative newcomer to the ACLS picture. Adenosine is an antiarrhythmic that works by slowing the initiation of SA node impulses and blocking AV conduction reentry. This action produces a decrease of reentry arrhythmias such as paroxysmal supraventricular tachycardia (PSVT).

Adenosine is indicated for the treatment of PSVT and it is the dug of choice in narrow-complex tachycardias. It may be used in wide-complex tachycardia of uncertain origin, but only after lidocaine has failed to slow the rate. In this situation, adenosine is used as a diagnostic drug with the hope that the heart rate will slow enough to allow a precise diagnosis to be made.

The usual dose of adenosine is 6 mg rapid IVP followed by 12 mg in one to two minutes if there is no response. The 12 mg dose may be repeated one time after one to two minutes, if needed. The maximum dose is 30 mg. An important fact to keep in mind regarding adenosine is that it has an extremely short half-life (<10 seconds) and must be administered rapidly (in one to three seconds) through an IV port closest to the patient. After administration, adenosine should be followed by a normal saline flush. A stopcock setup with normal saline already attached to the IV site is recommended.

Because adenosine slows AV conduction, it is contraindicated in patients with second- or third- degree AV blocks who do not have artificial pacemakers. In addition, adenosine is contraindicated in patients taking theophylline derivatives, carbamazepine (Tegretol), or dipyridamole (Persantine). These drugs may interfere with the action of adenosine; therefore, other drugs should be considered.

When administering adenosine, you must observe the cardiac monitor closely for momentary periods of asystole, sinus bradycardia, or ventricular ectopy. Your patient may also experience periods of dyspnea, chest pain, or flushing. These symptoms are usually short-lived and generally disappear within a few minutes. However, emergency equipment should be immediately available.

Other Emergency Aaents

Dopamine, commonly used after establishing a normal sinus rhythm and prior to transferring the patient to a critical care unit, is an inotropic vasoactive agent. This drug is always administered via IV drip with a usual concentration of 400 mg in 250 cc DSW. Its actions are dose-related.

In low doses (1 mcg kg/min to 2 mcg kg/min), dopamine dilates renal arteries and improves renal perfusion. In large doses (2.5 mcg/kg/min to 20 mcg/kg/min), it augments cardiac output by increasing heart rate, myocardial contractility, and stroke volume and raises blood pressure by causing peripheral vasoconstriction. If doses greater than 20 mcg/kg/min are needed to maintain an adequate blood pressure, norepinephrine should be administered simultaneously.

Bretylium is used to treat ventricular fibrillation and ventricular tachycardia that is unresponsive to lidocaine. The initial dose is 5 mg/kg and subsequent doses of 10 mg/kg may be repeated every five minutes up to a maximum dosage of 35 mg/kg. Its major adverse reaction is hypotension, although nausea and vomiting may occur. Bretylium is contraindicated for patients with digitalis toxicity.

Procainamide is also indicated for ventricular fibrillation or ventricular tachycardia that is not controlled by lidocaine. A usual loading dose is 20 mg/min to 30 mg/min to a maximum dose of 17 mg/kg IV, followed by a continuous IV infusion at 1 mg/min to 4 mg/min. Remember to discontinue the loading dose as soon as it is effective and begin the continuous infusion to avoid toxicity. Closely monitor patients receiving this drug for changes in blood pressure and adverse reactions such as widening of the QRS complex and lengthening of the PR and QT intervals. If the QRS complex widens by greater than 50% of the predrug administration width, discontinue the medication.

Sodium Bicarbonate should only be administered when there is documented hyperkalemia or metabolic acidosis. The best way to correct acidosis is through aggressive CPR and ventilation. Usually supplied in a 50 cc syringe containing 50 mEq, an initial dose is 1 mEq/kg, until a more appropriate dosage can be calculated to arterial blood gas findings.

Macgnesium Sulfate (MgS04), a recent addition to the ACLS algorithms, is an electrolyte that regulates the movement of calcium in and out of cells. Because calcium is necessary for cardiac contraction, deficiencies in magnesium disrupt the function of calcium, which can cause cardiac dysrhythmias such as refractory ventricular fibrillation and torsade de pointes, a form of ventricular tachycardia.

When MgS04 is administered in a code blue situation, the usual dose is 1 gm to 2 gms in 10 cc D5W given over one to two minutes. MgS04 may also be given prophylactically for the acute MI patient with confirmed hypomagnesemia to decrease ventricular ectopy; this dose is 1 gm to 2 gms in 100 cc over 50 to 60 minutes followed by a 24-hour infusion of 0.5 gm/hour to 1 gm/hour. Rapid administration can produce significant hypotension and asystole, as well as a prolonged PR interval and a widened QRS complex. Patients may also develop flushing, respiratory depression, heart blocks, and loss of deep tendon reflexes. The treatment of MgS04 toxicity is calcium gluconate.

Calcium Chloride is an electrolyte that increases the force of myocardial contractions when an orderly, but ineffectual rhythm has been established; it is also indicated for hyperkalemia, hypocalcemia, or calcium channel blocker toxicity. The dose is 8 mg/kg to 16 mg/kg of a loo solution; generally, 1 gm is given IVP (10 cc). Precautions must be taken with patients who are digitalized because calcium increases ventricular irritability and may precipitate digoxin toxicity.

Administration

Medications are given primarily intravenously during a code; however, certain drugs, such as epinephrine, atropine, and lidocaine, may be given via the endotracheal tube in the absence of IV access. When administering via this route, the dose should be 2 to 2 . 5 times the normal IV dose. The medication should be diluted in 5 cc to 10 cc normal saline, instilled into the tube, and followed by positive pressure ventilations to promote bronchial absorption.

Golden Rules

Most emergency drugs are given during a code. A few guidelines can ensure that their administration is orderly, accurate, and appropriate.

- Treat the patient and not the monitor. For example, ventricular tachycardia in a conscious patient is treated differently than if the patient were pulseless and unconscious.
- Organize the code. Everyone should have a role and stick to it; for example, medication nurse, recording nurse, patient care nurse. Locate medications and learn how to use equipment before the code. Practice setting up oxygen and suction apparatus and become familiar with using the defibrillator to quickly establish the patient's rhythm.
- Participate in mock codes.

- Document accurately. Record the events leading up to the code, when CPR was begun, and when defibrillation was performed.
- Clearly identify rhythms, their treatment, medications, and the patient's responses. Record vital signs frequently. Sign the code form legibly and include the names of key code members, if that is the policy at your institution.
- Take care of the family. Remember that the patient's family will be terrified and, in the event of death, they will be grieving.
- Find a support person, such as a psychiatric liaison or staff nurse, chaplain, or social worker, to stay with them. The patient's physician will need to speak with them as soon as possible. Families appreciate knowing, in gentle language, what is going on during the code. The code and patient care teams will also need support.

Emergency drug therapy plays a key role in the survival of code blue patients. Nurses in clinical areas need to be competent in BLS and familiar with emergency drugs and their use in accordance with ACLS protocols.

Other Cardiovascular Updates

Vascor,

Bepridil, a new calcium channel blocker is up for approval by FDA. It will be marketed by McNeil Pharmaceuticals as a treatment for chronic stable angina pectoris. It has a much longer effect than all other calcium blockers so far. Patients will take the drug only once a day in 300mg to 400mg doses.

So far, studies have shown that the drug significantly reduces the frequency of angina attacks and the consumption of nitroglycerin tablets. The side effects are nausea, dyspepsia, diarrhea, dizziness and nervousness, not unlike the side effects of many of the other calcium blockers. The company also reports that this drug may be safely used in combination with other drugs commonly used by these angina patients.

Short-term CHF Management-

Amrinone lactate (Inocor), is used for short-term management of CHF in patients who have not responded to therapy with digitalis glycosides, diuretics, and vasodilators. Inocor produces inotropic action in the heart and also produces vasodilation through a direct relaxation effect on vascular smooth muscle. Dosage is 0.75 mg/kg IV bolus over 2-3 minutes, initially; then a 5-10 mcg/kg/minute as a maintenance dose.

Nursing considerations:

a. arrhythmia, hypotension--monitor blood pressure/heart rate during infusion **b. GI symptoms--nausea,** vomiting, cramps, dyspepsia, diarrhea
c. thrombocytopenia--monitor platelet count, if the count becomes lower than 150,000 mm', then decrease dosage
d. do not mix with other drugs--do not mix with dextrose solutions; may be injected in free-flowing dextrose IV, do not let stand in dextrose solutions

Newer Antihypertensives:

1. Guamfacine hydrochloride, (Tenex, Robins), is a centrally acting alpha2adrenergic receptor agonist. Its antihypertensive action is similar to that of clonidine (Catapres) and methyldopa (Aldomet). It is usually administered in one daily dosage, because it is so long-acting. Usually the drug is well tolerated and side effects are minimal. Nursing considerations: inform patient that it may make him drowsy or dizzy. Due to these side effects, drug should be taken at bedtime to reduce the symptoms. Blood pressure and pulse should be monitored. The drug may also lower the tolerance to alcohol. Warn patient not to discontinue drug abruptly. This may cause nervousness, anxiety, or rebound hypertension in 2-4 days.

2. Terazosin hydrochloride, (Hytrin, Abbott, Burroughs Wellcome), is a selective alpha, -adrenergic blocker similar to prazosin (Minipress).

It can be used alone or in combination with other antihypertensive drugs. The drug is a vasodilator of relatively long-acting duration and can usually be administered once a day. Nursing considerations include: warn patient about orthostatic hypotension, and to rise slowly out of bed. Other precautions include: monitor pulse, blood pressure, avoid activities that might require alertness, the drug might make patient drowsy; do not interrupt therapy once started, and do not miss even a single dose if at all possible (unless directed by MD).

3. Perindopril erbumine (Aceon, Solvay) is the loth angiotensin-converting enzyme (ACE) inhibitor to be marketed to treat essential hypertension. Like other ACE inhibitors, it decreases vasoconstriction, decreases aldosterone secretion, lowers blood pressure, and is less effective in black patients than in white patients. It can be used alone or in combination with other antihypertensive drugs, such as a thiazide diuretic.

Precautions: (1) Contraindicated in patients with a history of angioedema related to previous treatment with an ACE inhibitor. Use caution in patients with a history of angioedema unrelated to ACE inhibitors. (2) Contraindicated in the second and third trimesters of pregnancy. ACE inhibitors can cause fetal injury and death. (3) Monitor for hyperkalemia in patients with renal impairment and diabetes and in patients also taking a potassium-sparing diuretic. Avoid concurrent use of perindopril and potassium-sparing diuretics if possible. (4) Monitor patients with preexisting renal impairment and those taking a diuretic for changes in renal function. (5) Monitor for lithium toxicity in patients taking both perindopril and lithium.

4. Eprosartan mesvlate is the sixth angiotensin II receptor antagonist to be marketed, eprosartan mesylate (Teveten, Unimed) is indicated to treat hypertension, either alone or in combination with other antihypertensive drugs, such as diuretics and calcium channel blockers. Unlike ACE inhibitors, angiotensin II receptor antagonists don't break down bradykinin, so they're unlikely to cause coughing, a common adverse effect of ACE inhibitors. Like ACE inhibitors, angiotensin II receptor antagonists are generally less effective in black patients than in white patients.

Precautions: (1) Use caution in patients with impaired renal function or a risk of impaired renal function; for example, because of renal artery stenosis or severe heart failure. Eprosartan may cause changes in renal function. (2) Symptomatic hypotension may occur in patients who are salt- or volume-depleted (for example, patients taking diuretics). (3) May cause fetal injury or death in the second and third trimester of pregnancy. Adverse reactions: upper respiratory tract infection; rarely, elevated serum potassium concentrations, facial edema.

DRUG FOR INTERMITTENT CLAUDICATION - Cilostazol

Getting patients back on their feet. The first drug approved for intermittent claudication in 15 years, cilostazol (Pletal, Otsuka; Pharmacia & Upjohn) joins pentoxifylline as treatment for this disorder. Cilostazol reduces symptoms of intermittent claudication, allowing patients to walk greater distances and increasing the time to initial pain (known as pain-free walking distance). For some patients, the improved walking distance is the equivalent of two or three blocks, which can mean the difference between being homebound and participating in everyday activities.

Cilostazol apparently relieves symptoms of intermittent claudication by inhibiting platelet aggregation and causing vasodilation. Studies suggest that it's a more potent antiplatelet agent than aspirin, dipyridamole, ticlopidine, or pentoxifylline. In contrast, the older drug for intermittent claudication, pentoxifylline, relieves symptoms by improving capillary blood flow and decreasing blood viscosity.

Use caution if the patient is also taking aspirin or warfarin because of the potential for bleeding (although this wasn't a problem in limited studies). Because many people with peripheral arterial disease take drugs with antiplatelet activity, research is under way to determine the risks and benefits of these combinations.

Grapefruit juice and various drugs inhibit the pathways that metabolize cilostazol, increasing plasma concentrations of cilostazol. Advise patients taking cilostazol to avoid grapefruit juice and closely monitor concurrent therapy with drugs such as erythromycin, ketoconazole, fluoxetine, and omeprazole. See the package insert for a complete listing of possible interactions and precautions.

Adverse effects associated with cilostazol include headache, diarrhea, abnormal stools, dizziness, and palpitations. For most patients, adverse reactions are mild to moderate.

The recommended dosage is 100 mg twice a day, taken at least 30 minutes before or 2 hours after breakfast and dinner. The dosage may be reduced to 50 mg twice a day in patients taking drugs that inhibit cilostazol metabolism.

Instruct the patient to take cilostazol apart from meals and inform him that he may not experience the drug's full benefits until he's been taking it for up to 12 weeks (although some patients improve significantly within 2 weeks).

RESPIRATORY DRUGS UPDATE

NEWER ANTIHISTAMINES:

a. Loratidine (Claratyne, Claritin), is a new antihistamine drug that is being marketed as being non-sedating, and long-acting. This drug in clinical trials has proved to be as effective as other antihistamines and is non-sedating. It has shown not to cause the sedation as other antihistamines. This drug is also four times more potent as other antihistamines. Therefore, it can be taken only once a day. The daily dosage is 10 mg. In higher doses the drug is found to cause impairment, but still has no sedative effects. This drug has also been found to be effective for up to 28 days continuous use. Other antihistamines will lose their effectiveness in a very short period of time (one week).

b. Dexchlorpheniramine (Dexchlor, Poladex TD, Polaramine), AND ....

c. Methdilazine (Dilosyn, Tacaryl), are both new antihistamines similar to others in their class. They have the same precautions of **drowsiness, dizziness, dry mouth, urinary retention,** just as other similar antihistamines.

Ketotifen fumarate

A relatively selective histamine antagonist and mast cell stabilizer, ketotifen fumarate (Zaditor, Ciba Vision) is provided in an ophthalmic solution indicated to temporarily prevent itching eyes from developing into allergic conjunctivitis. The most common type of ocular allergy, allergic conjunctivitis affects an estimated 50 million people.

The most commonly experienced adverse effects, headache, redness, and rhinitis, are usually mild. Uncommon adverse effects include allergic reactions, burning or stinging, discharge, dry eyes, eye pain, itching, keratitis, lacrimation disorder, mydriasis, photophobia, and rash. Systemic effects are unlikely. .

The recommended dosage is one drop in the affected eye or eyes twice a day every 8 to 12 hours. Teach the patient the proper technique for administering eyedrops. Also warn her that the medication may ruin soft contact lenses. She shouldn't administer the drops while wearing soft contact lenses, and she should wait at least 10 minutes before reinserting them. Advise her not to wear contact lenses if her eyes are red; also inform her that ketotifen isn't a treatment for contact lens-related eye irritation.

NEWER BRONCHODILATORS:

a. ethylnorepinephrine hcl (Bronkephrine),
b. ipratropium bromide (Atrovent),
c. salmeterol xinafoate (Serevent)

These are the newer BRONCHODILATORS being used today. There uses and side effects are similar to aminophylline and epinephrine drugs.Side effects include **tachycardia, palpitations, headache, tremors, nausea, cough,** and others. These above drugs may be used for long-term management of asthma as well as for acute disease.

Theophylline/Food Update:

Recent studies show that food can greatly affect the absorption rate of all the oral theophylline preparations. One study showed that a high fat meal with ingestion of the theophylline will increase the amount of drug absorbed by up to 100%. Other studies show that foods will interact in many different ways.

Recommendations are to always follow manufacturer's instructions as to foods, and to always be consistent. Tell patients to always take their theophylline the same way all the time. Some take it on an empty stomach, some before a meal, some after a meal; Be consistent!

Flonase (fluticasone propionate) Nasal Spray, GlaxoWellcome

Flonase Nasal Spray, 0.05 is indicated for use in allergic rhinitis. It is a new drug designed to be used once in 12 to 24 hours and have a cumulative effect in controlling stuffy nose symptoms. Side effects include nasal irritation, nosebleeds, and headaches. Since this drug is intended for fairly long-term therapy, patients using this drug may be susceptible to certain infections. See the prescribing information supplied by the manufacturer for the list of warnings.

NEW ANTI-ASTHMA DRUG

ZAFIRLUKAST, first in its class; Zafirlukast (Accolate, Zeneca), the first of a new class of agents for treating asthma, is designated as a leukotriene receptor antagonist. Leukotrienes are mediators in the inflammatory process that contribute to the signs and symptoms of asthma. Zafirlukast inhibits bronchoconstriction caused by some leukotrienes.

Administered orally, zafirlukast is indicated for the prophylaxis and treatment of chronic asthma in adults and in children 12 years and older. In clinical studies in patients with mild to moderate asthma, the new drug improved daytime asthma symptoms, nighttime symptoms causing awakening, morning asthma symptoms, and.rescue beta2-agonist use (for example, albuterol [Proventil, Ventolin]). Researchers are still studying the potential benefits of zafirlukast for patients with severe asthma.

Precautions: (1) Warn your patient not to use zafirlukast to treat acute episodes of asthma. However, tell him that he can continue treatment with zafirlukast during acute exacerbations of asthma. (2) Concurrent use of aspirin may increase plasma concentrations of zafirlukast; concurrent use of erythromycin or theophylline may decrease them. (3) Exercise caution when this drug is used concomitantly with carbamazepine (Tegretol) or phenytoin (Dilantin) because these drugs are metabolized via the same pathway. (4) Use caution if the patient is also taking warfarin, and monitor prothrombin times (PTs) carefully. Concurrent use of zafirlukast with warfarin increases the half-life of warfarin and increases the PT. (5) Zafirlukast should be used during pregnancy only if clearly needed. It's excreted in human milk and shouldn't be administered to women who are breast-feeding.
Adverse reactions: headache, infections, nausea, diarrhea. Supplied as: 20 mg tabs.
Dosage: 20 mg twice a day.
Nursing considerations:(1) Closely monitor PT in those who are also taking warfarin so that anticoagulant dosage can be adjusted. (2) Teach patient to take zafirlukast at least 1 hour before or 2 hours after meals. (3) Tell him that his asthma symptoms should improve within 1 week of starting treatment with zafirlukast.

Oseltamivir phosphate and Zanamivir -- Flu fighters

Every year, about 300,000 Americans are hospitalized for influenza, and some 20,000 die. Two new antiviral drugs, oseltamivir phosphate (Tamiflu, Roche) and zanamivir (Relenza, Glaxo Wellcome) are indicated for uncomplicated acute influenza infection in patients who've been symptomatic for no more than two days.

Classified as the first neuraminidase inhibitors to be marketed in the United States, the new drugs bind to and inhibit the action of a viral enzyme that facilitates the spread of viruses from cell to cell. This limits tissue damage and the duration of symptoms. Unlike amantadine and rimantadine, drugs previously marketed for influenza, the new drugs are active against both influenza A and B. The new drugs are also less likely to cause adverse reactions than the older drugs and may be less likely to promote the emergence of resistant influenza strains. Recent clinical studies indicate that the new drugs may help prevent as well as treat influenza, although prophylaxis isn't yet a labeled indication.

Zanamivir is administered by oral inhalation, so it's more likely to cause respiratory adverse reactions than oseltamivir, an oral drug. However, zanamivir is less likely to cause systemic adverse reactions, making it a better choice for pregnant women. In general, both drugs are well tolerated.

Tell patients that the new drugs are most effective when taken as soon as possible following the onset of symptoms. Also stress that these drugs are not substitutes for influenza immunization and that they should continue to receive an annual vaccination as advised by their health care provider.

Oseltamivir phosphate

In placebo-controlled trials, the median time to symptom improvement in patients receiving oseltamivir was reduced by 1.3 day (30%). Precaution: Because the drug is eliminated via renal excretion, reduce the dosage in patients with impaired renal function (creatinine clearance below 30 ml/minute). Adverse reactions: nausea, vomiting

Zanamivir

Delivered via oral inhalation, zanamivir reduced the duration of major influenza symptoms by 1 to 2-1/2 days in clinical trials. The drug was effective only in patients who initiated treatment within 2 days of symptom onset. Patients considered at highest risk for influenza, such as the elderly, experienced the most pronounced benefits.

Precautions: (1) A patient with underlying pulmonary disease may experience bronchospasm or a decrease in lung function. Advise him to have a fast-acting inhaled bronchodilator available when using zanamivir. (2) If respiratory symptoms worsen following use of zanamivir, the patient should discontinue the drug.

Adverse reactions: nausea, diarrhea, headache, dizziness, respiratory effects (sinusitis, bronchitis, cough, nasal symptoms, infections)

Dosage: two inhalations (one 5-mg blister per inhalation for a total of 10 mg per dose) twice a day for five days.

Nursing considerations: (1) warn a patient with chronic obstructive pulmonary disease about the potential for adverse respiratory effects and instruct him to keep a fast-acting inhaled bronchodilator (such as albuterol) at hand. (2) Demonstrate how to use the delivery system. See the package insert for details. (3) Instruct the patient to take two doses on the first day of treatment, with at least 2 hours between doses. on subsequent days, he should administer doses about 12 hours apart (for example, in the morning and evening) at about the same time each day. (4) Tell him to complete the 5-day course of treatment, even if he begins feeling better. (5) If he uses an inhaled bronchodilator at the same time as zanamivir, tell him to use the bronchodilator first. (6) Instruct him to stop taking the drug and call his health care provider if respiratory symptoms worsen during treatment.

MUSCULOSKELETAL DRUGS UPDATE

Treatment of early stage MS

Linoleic acid has been used successfully to treat the early stages of MS. Patients on this drug seem to have less severe and shorter relapses when treated early in the disease. Patients with more advanced stages of the disease failed to respond to drug (and most others).

Tizanidine (Zanaflex) New spasticity agent (AJN)

Zanaflex was approved in December 1996, and is the first new oral drug for muscle spasticity to enter the marketplace in more than 20 years. This drug is useful for treating muscle spasticity that often accompanies paralysis after a traumatic spinal cord injury.

It also often occurs in multiple sclerosis or upper motor neuron lesion that causes an abnormal increase in involuntary muscle tone. The affected muscles in the latter often contract spontaneously. This leads to painful muscle spasms with increased reflexes. Difficulty controlling the muscles results in functional defects. For example, leg spasms, occurring spontaneously, upon trivial stimuli, or following noxious stimuli (such as from a full bladder or bowel), can interfere with eating, sitting, walking, or sleeping. Spasticity may also complicate transfer in and out of a wheelchair.

In addition to nonpharmacological measures such as range of motion exercises and surgical interventions, several medications are used to alleviate debilitating spasticity:

- Baclofen--interferes with release of exictory neurotransmitters, reduces the number of spasms, and relieves stiffness in the legs, but weakens muscles in up to 150 of patients.
- Dantrolene (Dantrium) acts directly on skeletal muscle by interfering with the action potential-induced release of calcium ions from the muscle cell. It may cause muscle weakness and, at high doses, serious hepatotoxicity.
- Diazepam relaxes skeletal muscles by inhibiting spinal polysynaptic afferent pathways. But treatment requires the patient to understand the drug's abuse potential and the danger of using alcohol while on the drug. The drug may also cause depression and withdrawal symptoms.

New use for Enbrel

A new use for ENBREL(R) (etanercept) was approved by the FDA. This new, expanded indication for ENBREL for reducing signs and symptoms and delaying structural damage in patients with moderately to severely active rheumatoid arthritis.

The FDA approved ENBREL on November 2, 1998 to treat moderately to severely active rheumatoid arthritis in patients who have an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).

USE CAUTION IN PATIENTS PREDISPOSED TO INFECTION. The most frequent adverse events in placebo-controlled trials in rheumatoid arthritis were injection site reactions (ISR), infections, and headache. Only the rate of ISR was higher than placebo. The most frequent adverse events in the ERA trial were infection, ISR, and headache. Only the rate of ISR was higher than methotrexate. In all RA patients treated in clinical trials, malignancies were rare. In clinical trials, frequency of serious adverse events was 4!~ EN13REL compared to 5% placebo; and 6s ENBREL compared to methotrexate.

Enbrel acts by binding tumor necrosis factor (TNF). TNF is one of the dominant cytokines or proteins that play an important role in normal immune function and the cascade of reactions that cause the inflammatory process of RA. ENBREL competitively inhibits the binding of TNF molecules to the TNF receptor (TNFR) sites. The binding of ENBREL to TNF renders the bound TNF biologically inactive, resulting in significant reduction in inflammatory activity.

Celecoxib and Rofecoxib

Two new NSAIDs, celecoxib (Celebrex, Searle; **Pfizer) and rofecoxib (Vioxx,** Merck), offer safer therapy for patients with inflammatory disorders, they represent an important therapeutic advance.

Risks and precautions for these drugs are similar to those for other NSAIDs. For example, they're contraindicated for patients who've experienced asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs because of the potential for severe anaphylactic-type reactions. Even though serious GI effects are less likely with these drugs than with other NSAIDs, use caution in patients with a history of peptic ulcer disease or GI bleeding and in patients with factors that increase GI bleeding risks, including use of oral corticosteroids or anticoagulants, older age, smoking, and alcoholism.

Monitor patients for adverse renal reactions. Although experienced infrequently with NSAIDs, renal reactions are a risk for those using NSAIDs on a long-term basis (for example, to treat arthritis), the elderly, those with impaired renal or hepatic function or heart failure, and those taking a diuretic or an angiotensin-converting enzyme (ACE) inhibitor. The new drugs aren't recommended for patients with advanced kidney disease.

Fluid retention and edema are also potential problems, so use these drugs cautiously in patients with fluid retention, hypertension, and heart failure. Dehydrated patients should be rehydrated before starting therapy with celecoxib or rofecoxib.

The risk of hepatic reactions seems low, but closely monitor patients with signs and symptoms of liver dysfunction. Unlike aspirin and other older NSAIDs, celecoxib and rofecoxib don't inhibit platelet aggregation, so they're not appropriate as a substitute for aspirin for cardiovascular prophylaxis. The new drugs don't increase bleeding times or generally affect platelet counts and may be used concurrently with low-dose aspirin. However, aspirin increases the risk of GI effects.

Like other NSAIDs, celecoxib and rofecoxib decrease the antihypertensive effect of ACE inhibitors, decrease the diuretic effect of thiazide diuretics and furosemide, and increase serum concentrations of lithium. Concurrent use with an aluminum- and magnesium-containing antacid, such as Maalox, may significantly reduce plasma concentrations of both new drugs. Women shouldn't take either drug during the third trimester of pregnancy because these drugs could trigger premature closure of the ductus arteriosus.

Here are some specific considerations for each drug:

Celecoxib is indicated for relief of symptoms of osteoarthritis and rheumatoid arthritis. Within a short time following its marketing launch in early 1999, celecoxib had become the most widely prescribed brand-name medication for the treatment of arthritis and had set records for the number of new prescriptions and refills dispensed. This reflects an expectation that the new drug will be as effective as other NSAIDs with fewer adverse reactions.

A particular concern with this drug is the similarity of its trade name, Celebrex, with Celexa (the trade name for the antidepressant citalopram) and Cerebyx (the trade name for the antiseizure drug fosphenytoin). Many drug errors stemming from these similarities have been reported.

Precautions (besides those discussed previously for both drugs):

(1) Contraindicated for patients who are allergic to sulfonamide antibacterial drugs, such as sulfamethoxazole. Celecoxib contains a similar component that creates the potential for cross-reactivity in susceptible patients.
(2) If celecoxib and warfarin are used concurrently, monitor the anticoagulant response closely during the first few days after initiating or changing celecoxib therapy to prevent bleeding complications.
(3) Concurrent use of celecoxib and fluconazole (Diflucan) may double plasma concentrations of celecoxib; treatment with celecoxib should be initiated with the lowest recommended dosage in patients receiving both drugs.
(4) Initiate celecoxib therapy at a reduced dosage in patients with moderate hepatic impairment and monitor liver function. Celecoxib isn't recommended for those with severe hepatic impairment.
(5) Initiate therapy at the lowest recommended dosage in patients weighing less than 110 pounds (50 kg).

Adverse reactions: headache, upper respiratory tract infection, dyspepsia, diarrhea, abdominal pain. Supplied as: capsules in 100-mg and 200-mg potencies. Dosage: For osteoarthritis, use 200 mg/day as a single dose or 100 mg twice a day. For rheumatoid arthritis, use 100 to 200 mg twice a day.

Nursing considerations:

(1) Advise the patient that he can take celecoxib without regard to meals.

(2) Be aware of the risk of medication errors related to trade-name similarities.

Follow standard guidelines for administering medications to avoid misinterpreting an order.

Rofecoxib is indicated for relief of osteoarthritis, management of acute pain, and treatment of dysmenorrhea. Unlike celecoxib, rofecoxib shouldn't cause complications in patients who are allergic to sulfonamide antibacterial drugs. Also unlike celecoxib, rofecoxib is available as an oral suspension.

Precautions (besides those listed previously for both drugs):

(1) Not recommended for patients with moderate or severe hepatic impairment.
(2) In patients taking warfarin concurrently, closely monitor the anticoagulant response after initiating or changing rofecoxib therapy.
(3) Initiate therapy at the lowest recommended dosage in the elderly.
(4) The concurrent use of rifampin, a nonspecific enzyme inducer, may reduce rofecoxib plasma concentrations by 50%. A starting rofecoxib dosage of 25 mg is recommended for osteoarthritis.

Adverse reactions: upper respiratory tract infection, diarrhea, nausea, headache
Dosage: For osteoarthritis, 12.5 mg once a day initially. Dose may be increased to 25 mg once a day, the maximum recommended dosage for this condition. For acute pain and primary dysmenorrhea, use 50 mg once a day. (Use of the drug to treat pain for more than five days hasn't been studied.)

SKELETAL MUSCLE RELAXANT - Rapacuronium bromide

Categorized as a nondepolarizing neuromuscular blocking agent, rapacuronium bromide (Raplon, Organon) is indicated as an adjunct to general anesthesia to facilitate tracheal intubation and to provide skeletal muscle relaxation during surgery. It's the first nondepolarizing neuromuscular blocker to combine a rapid onset of action (about 90 seconds) with a short duration of action (about 15 minutes). Like other nondepolarizing neuromuscular blockers, such as pancuronium (Pavulon), rapacuronium is considered safer than succinylcholine, the rapid-acting depolarizing neuromuscular blocker also used to facilitate intubation.

Adverse effects associated with rapacuronium include hypotension, tachycardia, bradycardia, and bronchospasm. It must be used with caution in patients with myasthenia gravis or myasthenic syndrome, in patients receiving other medications that may increase or prolong neuromuscular block, such as inhalation anesthetics and certain antibiotics, and in patients with renal or hepatic impairment. Chronic use of anticonvulsant drugs such as carbamazepine (Tegretol) and phenytoin (Dilantin) may shorten rapacuronium's duration of action. See the product insert for a complete listing of precautions.

Rapacuronium is administered via I.V. injection (not infusion), in conjunction with an anesthetic or sedative. Don't induce neuromuscular block while the patient is conscious. Monitor her with neuromuscular monitoring equipment, such as a peripheral nerve stimulator, to assess the drug's effect, determine the need for additional doses, and confirm recovery from neuromuscular block. Support ventilation as indicated until she recovers from the blockade. If necessary, rapacuronium's effects can be reversed with neostigmine (Prostigmin).

The recommended initial dose for tracheal intubation is 1.5 mg/kg for short surgical procedures. In patients undergoing cesarean section, the recommended intubating dose with thiopental induction is 2.5 mg/kg. Following an intubating dose of 1.5 mg/kg, up to three maintenance doses of 0.5 mg/kg have been used, with the duration of neuromuscular blockade increasing with each dose. Don't give repeat doses until recovery of neuromuscular function is evident.

ONCOLOGY DRUGS UPDATE

The term chemotherapy is defined as a **systematic cancer treatment using certain** specific drugs to treat specific types of cancer. There are more than 100 drugs available today to treat cancer. There are many categories of drugs used to treat cancer. Some drugs are used specifically and exclusively for cancer treatment. Some drugs have uses other than for chemotherapy. Drugs such as hormones and antibiotics may be used as chemotherapy agents under certain circumstances.

Cancer chemotherapy is a constantly changing field. Almost every day there are new cancer treatments and new drug protocols developed. We update this course frequently, however, no intent is implied as to the finality of any information included in this text. Therefore, always confirm **and verify any drug orders for** chemotherapy prior to administration of these highly toxic drugs.

Chemotherapy is usually administered in cycles. The drug is administered in the maximum tolerable dose to the patient. The first cycle kills some of the cancer cells. Then, repeated doses (cycles) of the drug are administered. Hopefully, these repeated doses will kill more and more of the cancer cells, until they are all killed and the cancer is termed "cured." This is the ideal situation.

The GOAL of chemotherapy is to destroy all cancer cells without causing excessive damage to the body's normal cells. The PRINCIPLE of chemotherapy is to administer the maximum tolerable drug dose; then repeat the dose many times; even beyond the time when no cells are detectable. This is because there still may be some cancer cells that are not detectable by tests.

TYPES OF CHEMOTHERAPY AGENTS

CELL CYCLE SPECIFIC DRUGS

Cell cycle specific drugs are those drugs which act on the cell during one of the particular phases of reproduction. Due to this action, these drugs usually have to be administered more frequently than some of the other chemotherapy-drugs. Because they must be given more frequently, there is a greater chance that they will be more effective against cancer cells. Remember that each time a drug is administered, more cancer cells are killed. This category of drugs includes antimetabolites and the mitotic inhibitors.

(Antimetabolites)

These drugs include methotrexate, 6-mercaptopurine (6MP), 5-flourouracil (5FU), 6-thioguanine (6GT), cytosine arabinoside (Ara-C), FUDR, and 5-Azacytidine. These drugs "generally" are less toxic to the body than some of the other chemotherapy agents. These drugs may usually be safely administered with minimum side effects; although some people may still have the usual side effects of the chemotherapy agents.

(Mitotic Inhibitors)

These drugs work by preventing cell division by destroying the mitotic spindle. Examples include: vincristine (Oncovin), vindesine, vinblastin.

CELL CYCLE NONSPECIFIC DRUGS

These drugs attack the cancer cells during any phase of reproduction. Therefore, the drugs are dose-dependent. This means that the higher the dose you give, the more cancer cells will be destroyed. However, many normal cells will also be destroyed by these drugs. Therefore, the dose of the drug must be regulated very carefully. These are: alkylating agents, antitumor antibiotics, and nitrosoureas.

(Alkylatincr Agents)

This group of drugs prevents cell division by damaging the DNA of cells. Drugs in this category are: melphalan (L-PAM), nitrogen mustard, cyclophosphamide (Cytoxan), chlorambucil, busulfan (Myleran), thiotepa, estramustine, DTIC, hexamethylmelamine, cisplatinum, and carboplatin.

(Antitumor Antibiotics)

These antibiotics attack DNA similar to the alkylating agents. Drugs in this category include: Dactinomycin, doxorubicin (Adriamycin), daunomycin, bleomycin, mitomycin, and mithramycin. Mithramycin is only rarely used in chemotherapy today, but is useful for treating hypercalcemia.

(Nitrosoureas)

These drugs are special types of Alkylating agents. These drugs have a greater ability to attack cells in the resting phase. They also cross the blood-brain barrier. These drugs are streptozocin, methyl CCNU, BCNU, and CCNU. These drugs will tend to cause more severe side effects than other chemotherapy agents.. They also tend to damage normal cells due to their ability to attack ALL cells in the resting phase. Damaging the resting phase of ALL cells, means that normal cells and cancer cells will both be affected by these drugs.

MISCELLANEOUS AGENTS

PROCARBAZINE, HYDROXYUREA, AND L-ASPARAGINASE are three more agents that are used in chemotherapy. It is unknown how they work, but they are useful against a variety of cancers.

COMBINATION THERAPIES

In the actual practice of administering chemotherapy, the nurse will often encounter combination therapies. Very often the chemotherapy agents are given in combination for their combined effects. Over the years, it has been discovered that these certain combinations of agents just happen to work better in combination than when administered alone.

One common CHEMOTHERAPY combination is listed here:

M.O.P.P., is used for Hodgkin's Disease. The following drugs are given, usually in 4 cycles (courses) of 14 days, as follows:

M = Nitrogen Mustard	given IV,	days 1 & 8
O = Vincristine (Oncovin)	given IV,	days 1 & 8
P = PROCARBAZINE	given PO,	days 1-14
P = Prednisone	given PO,	days 1-14

(prednisone on 1st & 4th course only)

There are many other similar combination therapies used for different cancers. Always check the protocol used at your facility prior to administration of these drugs. The dosages are calculated according to each patient's height, weight, previous history and other factors.

OTHER INDIVIDUAL ONCOLOGY DRUGS AND UPDATES:

Marinol, now approved as an oral antiemetic. The FDA recently approved Marinol, dronabinol for use when other such agents fail. The only approved use of this Marijuana derivative is in oncology. It is used to control very severe nausea and vomiting experienced by patients who take chemotherapeutic agents. This drug, also called delta-9-THC, is the psychoactive substance in Marijuana.

Adverse reactions:

include drowsiness, dizziness, confusion, impairment of thinking and perceptions. Patients are warned not to drive or engage in activities requiring judgement and coordination. Nabilone (Cesamet) is also a marijuana derivative like Marinol-These drugs have a potential for abuse. Patients are warned to use the minimum needed to relieve the symptoms. Patients that go home, will also be limited in amounts given to them.

BICALUTAMIDE (Casodex, Zeneca)

Zeneca is a nonsteroidal antiandrogen drug indicated for treating advanced prostate cancer. The second leading cause of cancer deaths in American men, prostate cancer claims about 40,000 lives each year. Prostate cancer responds to treatment that counteracts or eliminates androgen.

About 95% of circulating testosterone can be removed by surgical castration or treatment with estrogen or a luteinizing hormone-releasing hormone (LHRH) agonist, which suppresses testicular androgen production by inhibiting luteinizing hormone secretion. However, these drugs don't suppress adrenal androgens, which can account for a significant concentration of androgen in prostate tissue.

Antiandrogens such as bicalutamide inhibit the action of androgens by binding to androgen receptors in the prostate. Combination treatment with an LHRH analogue such as goserelin acetate (Zoladex) or leuprolide acetate (Lupron) provides maximal adrogen blockade.

Bicalutamide may inhibit spermatogenesis; the long-term effects of the drug on fertility haven't yet been studied. Because bicalutamide is extensively metabolized in the liver, exercise caution in patients with moderate to severe hepatic impairment. Monitor serum prostate-specific antigen (PSA) regularly. If PSA levels rise during bicalutamide therapy, the cancer may be progressing. Bicalutamide can displace coumarin anticoagulants (for example Warfarin) from binding sites. So closely monitor PT's in these patients.

Advise your patient of the importance of using both bicalutamide and the LHRH analogue in the treatment regimen and of not interrupting or stopping either drug without consulting his physician. Teach him to take bicalutamide at the same time every day.

Docetaxel, Second-line drug for breast cancer

Docetaxel (Taxotere, Rhone-Poulenc Rorer) is the second taxoid antineoplastic drug marketed in the United States, joining paclitaxel (Taxol). Docetaxel promotes the assembly and inhibits the disassembly of microtubules in the cell, disrupting the microtubule network and reducing cell division.

Docetaxel is indicated for patients with locally advanced or metastatic breast cancer whose disease has progressed during anthracycline-based therapy (for example, with doxorubicin [Adriamycin]) and those who've relapsed during anthracycline-based adjuvant therapy. In clinical studies, docetaxel produced a higher tumor response rate than other drugs. It represents an important new therapy for this difficult-to-treat patient population. Docetaxel is being evaluated for ovarian cancer and lung cancer and as a first-line treatment for breast cancer. However, these aren't labeled indications at present.

Adverse reactions: bone marrow suppression, afebrile and febrile neutropenia, thrombocytopenia, bleeding, anemia, fluid retention, gastrointestinal reactions (for example, nausea, vomiting, diarrhea), fever in absence of infection, neurosensory symptoms (for example, paresthesias), rash, nail changes, alopecia, asthenia, stomatitis, myalgia, hypersensitivity reactions, elevated liver function tests

Supplied as: single-use vials containing 20 mg and 80 mg of the concentrated drug in 0.5 ml and 2 ml polysorbate 80, respectively

Dosage: 60 to 100 mg/m2 body surface area intravenously (I.V.) over 1 hour every 3 weeks

Gemcitabine Hcl, New weapon in oncology arsenal

Pancreatic cancer strikes about 26,000 people in the United States each year. It's one of the most difficult cancers to treat, in part because most patients don't develop symptoms until late in the course of the disease. Less than 100 of patients with pancreatic cancer survive more than 1 year after diagnosis. Chemotherapy (primarily with fluorouracil) has been of only limited benefit.

Gemcitabine HC1 (Gemzar, Lilly), the first drug for pancreatic cancer introduced in several decades, is a nucleoside analogue that competes with a natural component of DNA within the cell to inhibit DNA synthesis. Gemcitabine is indicated as first-line treatment for patients with locally advanced (nonresectable Stage II or Stage III) or metastatic (Stage IV) adenocarcinoma of the pancreas and as second-line treatment for patients who've previously received fluorouracil.

Although the benefits of gemcitabine are limited, the drug may be more effective than fluorouracil. In patients who hadn't previously received chemotherapy, the new drug was compared with fluorouracil for clinical benefit (defined as improvement in at least one of four clinical parameters [for example, pain intensity] for at least four weeks without deterioration in another) and survival. Gemcitabine provided a clinical benefit in 22% of patients (fluorouracil, 5%) and a median survival of 5.7 months (fluorouracil, 4.2 months). In patients who'd previously received fluorouracil, gemcitabine provided a clinical benefit in 27% of patients and a median survival of 3.9 months.

Gemcitabine is being evaluated as a treatment for non-small-cell lung cancer, ovarian cancer, breast cancer, and certain other malignancies; however, these aren't labeled indications at the present time.

IRINOTECAN HCL Important new advance

Irinotecan is indicated for patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following fluorouracil therapy. In studies, about 15% of patients experienced a reduction in tumor size.

The new drug represents an important advance; before its approval, no effective therapeutic alternatives existed for patients whose conditions progressed following fluorouracil treatment.

Diarrhea is one of the new drug's most important adverse effects. Irinotecan has caused both early and late forms of diarrhea (in 51% and 88% of patients, respectively). The two reactions appear to be mediated by different mechanisms. Early diarrhea (occurring during or within 24 hours of administration) is cholinergic in nature and may be preceded by diaphoresis and abdominal cramping. Although it can be severe, it's usually transient and treatable with atropine (0.25 to 1 mg I.V.).

Late diarrhea (occurring more than 24 hours after administration) can be prolonged, leading to potentially life-threatening dehydration and electrolyte imbalance. Late diarrhea should be promptly treated with loperamide (Immodium). However, prophylactic use of loperamide isn't recommended.

Precautions: (1) Assess white blood cell count with differential, hemoglobin, and platelet count before each dose. Therapy should be temporarily discontinued if the absolute neutrophil count drops below 500/mm3 or if neutropenic fever occurs. The dosage should be reduced if a clinically significant decrease in the total white blood cell count, neutrophil count, hemoglobin, or platelet count occurs. (2) Treatment can be restarted when the granulocyte count has recovered to 1,500/mm3 or more, the platelet count has recovered to 100,000/mm3 or more, and treatment-related diarrhea is fully resolved. (3) Consult the product labeling for specific recommendations for patients who develop serious adverse reactions. (4) Advise women of childbearing age to avoid becoming pregnant or breast-feeding while being treated with the drug.

NILUTAMIDE, New drug for prostate cancer

Nilutamide (Nilandron, Hoechst Marion Roussel) is the third nonsteroidal antiandrogen to be marketed in the United States, joining flutamide (Eulexin) and bicalutamide (Casodex) as treatments for metastatic prostate cancer. However, nilutamide is the first drug specifically indicated for use in combination with surgical castration (orchiectomy).

In clinical studies, orchiectomy plus nilutamide provided significantly higher rates of complete and partial disease regression, decreases in bone pain, and longer times to disease progression and death from prostate cancer than orchiectomy plus placebo. Nilutamide is available in Canada as Anandron but isn't available in Australia.

Precautions: (1) Nilutamide is contraindicated in patients with severe hepatic impairment or severe respiratory insufficiency. (2) Nilutamide may increase concentrations of phenytoin, theophylline, and warfarin; dosages may need to be adjusted or therapeutic alternatives substituted.

Adverse reactions: hot flushes, nausea, constipation, increased alanine aminotransferase, increased aspartate aminotransferase, dizziness, dyspnea, hypertension, urinary tract infection, abnormal vision, impaired adaptation to dark, interstitial pneumonitis. Supplied as: 50-mg tablets. Dosage: six tablets once a day (total daily dose of 300 mg) for 30 days, followed by three tablets once a day.

Denileukin diftitox

Diftitox is a new weapon against disfiguring skin lesions. Cutaneous T-cell lymphoma (CTCL) is a term for a group of low-grade non-Hodgkin's lymphomas involving malignant T cells that manifest initially as skin lesions. Persistent and difficult to control, the lesions can be disfiguring and may incapacitate the patient as the disease progresses. In the United States, fewer than 1,000 new cases are diagnosed a year.

A designated orphan drug, denileukin diftitox (Ontak, Ligand) is the first drug specifically indicated to treat recurrent CTCL in patients whose tumor cells express a particular protein. Administered I.V., denileukin achieved a partial or complete response (at least a 5001 reduction in tumor burden sustained for more than six weeks) in 300 of patients participating in the largest clinical trial.

Two clinical syndromes are associated with I.V. denileukin administration:

(1)Flu-like symptoms (fever and chills, asthenia, nausea, and vomiting, myalgia, arthralgia) occurred in 9101 of patients within several hours to days of the infusion. Most responded well to standard treatments, such as acetaminophen, antihistamines, and antiemetics.

(2)Acute hypersensitivity-type reactions occurred in 690 of patients within 24 hours of the infusion. In 20 of patients, the reaction was severe.

Monitor patients for signs and symptoms of hypersensitivity, such as hypotension, back pain, dyspnea, vasodilation, rash, chest pain or tightness, tachycardia, dysphagia or laryngismus, and syncope.

Denileukin is contraindicated in patients known to be hypersensitive to it, diphtheria toxin, or interleukin-2. Other reported adverse effects include hypoalbuminemia, vascular leak syndrome (characterized by two or three of these symptoms: hypoalbuminemia, hypotension, and edema), infections (possibly related to decreased lymphocyte counts associated with the drug), edema, headache, increased cough, anorexia, diarrhea, transaminase elevations, and (rarely) thrombotic events, pancreatitis, acute renal insufficiency, microscopic hematuria, hyperthyroidism, and hypothyroidism.

Valrubicin

This is an orphan drug for bladder cancer. Instilled into the bladder, valrubicin (Valstar, Medeva) is indicated to treat refractory carcinoma in situ (CIS) of the urinary bladder in patients for whom immediate cystectomy is unacceptable. Because candidates for valrubicin number less than 1,000 per year, it's a designated orphan drug.

In trials, only 18% of patients experienced a complete response. A patient should be informed about the risks of delaying cystectomy, which can lead to metastatic cancer. If he doesn't respond completely to treatment within three months or if CIS recurs, cystectomy should be reconsidered.

Valrubicin is contraindicated in patients hypersensitive to another anthracycline or Cremophor EL (a solubilizing agent), those with urinary tract infections, and those with small bladder capacity (treatment requires instilling 75 ml of solution).

Because valrubicin is administered intravesically, it's unlikely to cause systemic effects. It shouldn't be used in patients with bladder perforations or compromised mucosal integrity because these conditions would increase the risk of systemic effects.

Local adverse effects include urinary frequency, urinary urgency, dysuria, bladder spasm, hematuria, bladder pain, urine incontinence, and cystitis. Most occur during or shortly after instillation of the drug and resolve in one to seven days. Patients with preexisting irritable bladder symptoms have an increased risk of adverse reactions.

The drug is supplied in vials, which should be refrigerated. Let the vials warm to room temperature before administration. (Don't heat the vials.) If you see a waxy precipitate, warm the vial in your hand until the solution is clear.

The recommended dosage is 800 mg administered intravesically once a wqek for six weeks. Consult the product labeling for guidelines on diluting and instilling the drug.

When caring for a patient receiving valrubicin therapy, keep these points in mind:

- Explain the instillation procedure to the patient and answer his questions.
- Tell him to retain the drug for two hours if possible, to void at the end of two hours, and to drink plenty of fluids after treatment.
- Valrubicin is red. Tell the patient to expect red-tinged urine for 24 hours after treatment and to notify the physician if the discoloration lasts longer or if bladder irritation persists.
- A component of the valrubicin formulation may cause leaching from polyvinyl chloride products. Use only administration products recommended in the product labeling.
- Stress to the patient the importance of follow-up care and monitoring by his physician.
- Exercise caution when handling any antineoplastic drug.
- Consult the product literature for pregnancy and breast-feeding precautions.
- Advise women of childbearing potential to avoid pregnancy and men to refrain from sexual intercourse while being treated.

NEUROLOGICAL DRUGS UPDATE

Tracrium. Atracurium besylate,

This is a new neuromuscular blocking agent. It is being used during surgery for muscular paralysis and intubation. The effect is similar to other drugs being used, like Pavulon. However, the recovery time for Tracrium is only 20 to 30 minutes, about a third of the normal recovery time for this group of drugs.

Nursing Implications:

a. adverse effects--bronchospasm, hypotension, reflex tachycardia
b. acts in 3 to 5 minutes, nurse must be in attendance with resuscitation equipment if needed.
c. it is an intermediate-acting drug, less time than Pavulon for recovery, yet longer than Anectine, which will recover in about five minutes.
d. dosage: 0.4 to 0.5mg/kg weight

Fluoxetine HCL (Prozac--DISTA)

This is a fairly new oral antidepressant unrelated to other available antidepressants. It is believed to work by blocking CNS uptake of serotonin. The drug is metabolized in the liver. Therefore, persons with impaired liver function should have the normal dosage lowered. The most common **side effects** reported are: rash, itching, chills, increased appetite, weight loss, agitation, bronchitis, and rhinitis. Instruct patients not to take this drug in the afternoon, as it tends to cause nervousness and even insomnia.

Interacts with many other drugs: Flecainide, carbamazepine, vinblastine, insulin, oral hypoglycemic agents, lithium, tricyclic antidepressants, Dilantin, tryptophan, and others.

Recently, Prozac has become very popular and is in wide use today. However, there have also been many reported side effects and possible dependence upon this drug. Many other possible interactions have been suspected with the use of this drug. Many foods have to be avoided that contain tryptophan, such as meats, poultry, fish, liver, kidneys, eggs, nuts, peanut butter, broad beans, wheat germ, and others. The doctor and nurse must carefully explain all the possible adverse effects of this drug and impress upon the patient to report anything unusual.

Local Anesthesia Update: (ISMP, 1997)

Healthcare professionals know the hazards associated with the use of intravenous or inhaled anesthetics but tend to consider topical anesthetics relatively innocuous substances. That topical anesthetics like benzocaine, dyclonine and lidocaine are widely available in many over-the-counter products, such as Cepacol Anesthetic Troches and Sucrets Maximum Strength Lozenges, only increases perception of their safety. However, methemoglobinemia, a serious, and sometimes fatal adverse drug reaction may occur.

A hospital recently reported two cases of methemoglobinemia due to topically applied anesthetics to FDA's MedWatch Program. In the first case, a day-old infant was scheduled for circumcision. An hour before surgery, EMLA cream (eutectic mixture: lidocaine 2.5%, prilocaine 2.50) was applied. Three days later, the baby exhibited circumoral cyanosis, and oxygen saturation (Oz saturation) was noted to be 89-910 (normal 95-990). ABGs revealed a methemoglobin (metHb) level of 15.9% (normal <1.5% of total hemoglobin). After treatment with 0.3 mL of 1% methylene blue IV over five minutes, the baby stabilized.

In the second case, a 67-year-old patient was scheduled for bronchoscopy due to recurrent respiratory problems. Prior to the procedure, the patient received three sprays of Hurricane Spray (benzocaine 20%) and approximately 3 mL of topical lidocaine lo. Post-procedure, his Oz saturation fell to 80o. Blood tests revealed a markedly elevated metHb of 450. With appropriate treatment his metHb level had decreased to 2.6% by day three.

MetHb concentrations greater than 10 to 1S percent of total hemoglobin will cause cyanosis, and at levels >70%, patients have died. Methemoglobinemia occurs when iron in hemoglobin is oxidized to its ferric form. Unlike hemoglobin, methemoglobin binds so firmly with oxygen that less of it is available to tissues. It can be hereditary, but methemoglobinemia is typically acquired from drugs and chemicals, such as nitrites and aniline derivatives, which includes virtually all local anesthetics.

A recent study assessed the safety and efficacy of EMLA cream for neonatal circumcision. The methemoglobin concentrations of the neonates who received EMLA did not differ significantly from those of the control group, but methemoglobinemia has been reported previously with the use of EMLA cream. Methemoglobinemia has also occurred when an OTC vaginal cream was used to treat an infant's diaper rash.

Safe Practice Recommendation: Methemoglobinemia is easily treated. It is important to recognize the possibility of it when topical anesthetics are used. Tell patients not to use topical anesthetics in high doses, on excoriated skin. Use with caution in infants/geriatric patients, some of whom may be less likely to tolerate them.

Action may be necessary to prevent confusion between Roxanne's oral liguid opiate products: (ISMP)

Nursing staff on a long-term care/palliative care unit notified the hospital pharmacy that an order for 60 mg of Roxanole (morphine sulfate) liquid every four hours for pain had just been written for a patient with advanced AIDS. Pharmacy responded but dispensed a 30 mL bottle of Roxicodone Intensolo (oxycodone) instead of a 30 mL bottle of Roxanol. At least four nurses incorrectly administered 60 mg of oxycodone instead of 60 mg of morphine for 7 doses in a row. Since 30 mg of oral oxycodone is approximately equivalent to 30-60 mg of oral morphine, the patient received as much as twice the intended amount of opiate on each occasion. However, the patient did not experience any adverse effects. The error was later discovered by a nurse who herself had made the same error three weeks earlier.

Several factors probably contributed to this mix-up. Both opiate product names begin with °Rox." They may be stored right next to one another in alphabetical order. Both are packaged in 30 mL bottles. Both have a 20 mg/mL concentration and are colorless solutions. Both items are sold by Roxane Laboratories and use characteristic brown on white labels with a similar layout and identical fonts for label text. All of these similarities may have contributed to the most important problem of all: pharmacists and nurses did not read the container label before dispensing or administering oxycodone.

Similar problems have occurred in the past with another Roxane product, Roxicet (oxycodone 5 mg and acetaminophen 325 mg in 5 mL) which has been confused with Roxanol. A patient who was supposed to receive 10 mL of Roxicet, got 10 mL of morphine concentrate instead (200 mg). Another unrelated problem, but one that is at least as serious, is confusion between the 20 mg/mL Roxanol and Roxane's morphine oral solutions in concentrations of 10 mg/5 mL or 20 mg/5 mL. Mix-ups between these items have resulted in massive opiate overdoses.

Conscious Sedation / Analgesia

Health care delivery is changing rapidly. Surgeries previously requiring a hospital stay are now being done on an outpatient basis. Some procedures previously done with general anesthesia are now done routinely in outpatient clinics. Much of this activity is spurned by managed care; with hospitals, clinics and physicians trying to balance cost and deliver quality health care.

Professional nurses are asked to assume more responsibilities; sometimes requiring additional training. The use of an IV conscious sedation technique for certain surgeries and procedures has facilitated the shift from inpatient to outpatient status.

The term conscious sedation describes a state of depressed consciousness that retains the patients ability to maintain the airway independently and continuously and to respond appropriately to physical stimulation and verbal commands. The term conscious sedation is now considered a misnomer. It is being replaced by the more appropriate term "sedation and analgesia." There exists a dose-dependent continuum between minimal sedation, deeper sedation and general anesthesia. Any patient may progress from a level of light sedation to sedation/analgesia or even deep sedation without the intent or the knowledge of the qualified individual providing sedation care. The ability to recognize the distinctions between levels of sedation by continuous monitoring allows the nurse to assist in the safe administration of carefully titrated IV medication.

Because it isn't always possible to predict how a patient will respond to sedative medication, JCAHO now mandates that hospitals have a standard of care for patients undergoing procedures associated with conscious sedation/analgesia. They must have an updated housewide policy and procedure on conscious sedation and analgesia.

Goals of Conscious Sedation/Analgesia, medicate the patient until he/she is drowsy or actually closes their eyes and sleeps. The patient is easily aroused when called by name or gently shaken but soon drifts back to sleep if not further stimulated.

Optimal conscious sedation/analgesia is achieved when the patient:

- Maintains consciousness
- Independently maintains his/her airway
- Retains protective reflexes [swallow and gag]
- Responds to physical and verbal commands
- Is not anxious or afraid
- Experiences acceptable pain relief
- Has minimal changes in vital signs
- Is cooperative during the procedure
- Has some degree of amnesia for the procedure
- Recovers to baseline [preprocedure] status safely and promptly

RNs responsible for a patient receiving conscious sedation/analgesia should have:

- Knowledge of the pharmacology of agents given, their desired/undesired effects and the pharmacological antagonists for opiates and benzodiazepines.
- The ability to assess level of consciousness and protective reflexes [gag and swallow].
- The ability to operate and interpret pulse oximetry.
- Skills in oxygen delivery devices, airway assessment and management.
- Basic Life Support certification. ACLS may be preferred, possibly required by a health care facility, although not required by JACHO.
- Health care professionals with ACLS skills should be readily available.
- ECG certification of cardiac monitoring. Be able to recognize life threatening cardiac arrhythmias and other complications related to sedation/analgesia and initiate appropriate interventions for patients who require continuous ECG monitoring.
- Assess, recognize and intervene in the event of complications or undesired outcomes. Inform the physician of any subtle changes in the patients condition that may warrant ceasing the procedure

Agents Commonly Used For Conscious Sedation/Analgesia:

The IV medications commonly used for conscious sedation/analgesia include benzodiazepines and opioids. Administering small incremental doses of IV sedation/analgesic drugs until the desired level of sedation and /or analgesia is achieved is preferred over a single dose based of a patient's size, weight or age. Titrating to effect should be done because individuals vary in their response to similar doses.

Benzodiazepines:

This group of drugs can diminish skeletal muscle spasm, reduce anxiety, produce sedation and at high doses produce amnesia for the procedure. They exert their effect by binding to the GABA receptor complex in the central nervous system. In the central nervous system GABA is an inhibitory neurotransmitter. They provide no analgesia and the sedative effect is dose-dependent. The respiratory effect in dosages used for conscious sedation/analgesia is a decrease in tidal volume. The two benzodiazepines most often used for procedural sedation are midazolam [versed] and diazepam [valium]. Lorazapam [ativan] is occasionally used but can produce prolonged sedation.

Midazolam is recommended as a replacement for diazepam as the drug of choice for conscious sedation. It has been available since 1982. It is water soluble, associated with no pain on injection, rare risk of phlebitis, no active metabolites, gives excellent anterograde amnesia and has a rapid recovery profile. Midazolam has a rapid onset of action of 1 to 5 min., peaks at 20 to 60 min., duration is 2 to 6 hours and half-life is 1 to 12 hours.

IV. dose in a healthy adult< 60 years 0.5 mg - 2.5 mg increments

Allow at least 3 minutes between doses to assess the full effect A total dose of >5 mg. usually not necessary. Maximum total dose should be <10 mg.

Once sedation achieved, additional doses should be 25% of the dose required to produce sedation endpoint i.e. 0.25 mg -1 mg. IV dose in an adult >60 yrs, debilitated or chronically ill.

Danger of apnea is greatest in this class of patients. Dose increments should be smaller and rate of injection slower. 1 mg -1.5 mg. initially. Titrate slowlyno more than 1.5 mg over a 3-min. period.

Wait an additional 3 min. to evaluate the sedative effect. If additional drug needed give no more than 1 mg. over 3 min. Wait 3 min. between doses for the full sedative effect. Total doses >3.5 mg. are not usually necessary.

If narcotic premedication or other CNS depressants are used, these patients will require at least 500 less midazolam than young, healthy, nonpremedicated patients.

Diazepam is associated with a greater variation in effect and prolonged action with a second peak effect at 6-8 hrs. It's long half-life of 20-70 hrs. limits its use in procedures using conscious sedation/analgesia done as same day procedures. It has an active metabolite. It is insoluble in water, requiring organic solvents to be in stable IV form; therefore tends to have pain on injection and increased risk of thrombophlebitis at the site of injection. Its use is contraindicated in acute narrow angle glaucoma. Onset is 1-5min., peaks in 15-30 min. and duration is 15-16 hours.

Lorazepam is occasionally used for procedural sedation. Onset is 5-15 min., peak is unknown, and duration is 8-48 hrs and half-life is 10-20 hrs. The usual dose for sedation and relief of anxiety is up to 2mg. IV administered 15-20 min. prior to the procedure. This dose generally should not be exceeded in patients >50 yrs. If necessary, in adults <50 yrs maximum total dose is 4 mg. [if increased lack of recall about perioperative events is considered beneficial]. Dilute in 1:1 compatible solution immediately before administering.

For painless procedures it may be appropriate to use benzodiazepines alone to provide sedation and reduce anxiety. However; if a procedure is expected to produce pain, an analgesic must be added. It is important to add opioids in patients undergoing repetitive painful procedures. Managing pain adequately during the first procedure the patient experiences usually helps reduce the anxiety associated with future procedures. This can help to prevent the continual use of benzodiazepines for controlling anticipatory anxiety in these patients.

Opioids

The term opioid is now preferred to the word narcotic. Opioids act by binding to opioid receptor sites in the brain and spinal cord to block the production of neurotransmitters and thereby inhibiting the transmission of pain. Side effects of all opioids include euphoria, nausea, vomiting, orthostatic hypotension, bradycardia, pruritis, urinary retention and varying degrees of histamine release. The three most commonly used are Morphine, Fentanyl, and Meperidine.

Morphine:

Onset is 5-10 minutes, peak is 20 minutes, duration is 30-60 minutes; half-life is 2-4 hrs. respiratory depression may last longer than analgesia. Give 1-2 mg. increments over a 30 sec. period every 5-10 min. Its use in short procedures is somewhat limited by a delay in peak analgesic effect and a long elimination half-life. The histamine release often causes hypotension. A positive note is that with a longer duration of action it is more suitable for longer procedures and when pain is expected to continue after the procedure.

Fentanyl:

Onset is 1-2 min., peak is 3-5 min., duration is one hour. Dose is **0.5-2.0** micrograms/ kg, dilute to 10 micrograms/ml. and administer very slowly over 2-5 minutes. Give **25-50** microgram increments every **10-15** minutes. Rapid IV injection may cause chest wall rigidity.

Meperidine (Demerol):

Onset is 5-10 min., peak is **10-15** min., duration is 3-4 hrs., and half-life is 2-3 hrs. Dilute 10 mg. /ml., administer in 10 mg. increments every 5-10 min. Its metabolite [normeperidine] has central nervous system stimulating properties and can cause grand mal seizures, irritability, tremors, muscle twitching, jerking and agitation. Normeperidine has a half-life of **15-20** hrs. compared to meperidines half-life of 3 hrs. Eliminated by the kidneys, it shouldn't be used for patients with decreased renal function. It is contraindicated in patients with pre-existing convulsive disorders and patients with untreated hypothyroidism, Addison's disease, and benign prostatic hypertrophy or urethral stricture. Use with caution in patients with preexisting convulsive disorders and in patients with atrial flutter or other supraventricular tachycardias. Research shows that Meperidine is more likely than other opioid drugs to cause post-op delirium in patients of all ages. It is clearly not a first-line opioid analgesic for the management of any type of pain. It's ordered use should be questioned.

Benzodiazepine and Opioid Combinations

All opioids produce direct depression on brainstem ventilation. Opioids depress the hypercarbic respiratory drive. They decrease minute ventilation chiefly by decreasing respiratory rate to the point of apnea with little effect on tidal volume. This process is dose dependent. If combining agents, the decrease in respiratory rate and decrease in tidal volume [benzodiazepine] will increase the risk of respiratory depression. Initial doses of both agents need to be decreased; with a **25-30%** decrease in the benzodiazepine dosage. If excessive sedation occurs during a procedure, decrease the dose of benzodiazepine before decreasing the dose of opioid to decrease the risk of losing pain control.

Reversal Agents

These groups of drugs have serious side effects and should be reserved for emergency situations or inadvertent overdose. Antagonists should be readily available but rarely used. Sedative/analgesics should be properly titrated so that reversal agents aren't needed.

Opioid Antagonists Naloxone [narcan] Onset: 1-2 min. Duration: **30-45** min. Half-life: Approximately 1 hr. Dilute 0.4 mg in 10 ml. normal saline giving no more than 0.5 ml. over 2 min. May give up to 0.8 mg.

The goal is to reverse the respiratory depressant effect of opioids. If too much is given too rapidly analgesia is reversed. Always titrate to effect.

Side effects: nausea, vomiting, hypertension, hypotension, tachycardia, sweating, ventricular arrhythmias.

Nalmefene [revex]

Onset: 1-2 min.
Duration: long, up to 6 hrs.
Half-life: approximately 10 hrs.
0.25 mcg/kg. slowly. Repeat in 2-5 min. intervals to a maximum dose of 1 mcg/kg. dilute and titrate to effect.

A single dose of nalmefene is usually enough to reverse most opioids, unlike naloxone that may need to be repeated because its duration of action is shorter than the duration of the opioid. A disadvantage is ineffective pain control after administration because its, duration of action is longer than most of the opioids it is meant to reverse.

Benzodiazepine Antagonist Flumazenil [romazicon]

Administer 0.2 mg. over 1-3 min. Repeat 0.2 mg. if desired response is not attained after waiting an additional 45 sec. Repeat at 1 min. intervals to a maximum dose of 1 mg.

If excessive sedation recurs, doses may be repeated every 20 min. to a maximum of 3 mg. in any one hour. If the patient doesn't respond to cumulative dosing of 1-5 mg. over 2-10 min., look for other causes of increased sedation. Can cause life-threatening seizures in patients receiving benzodiazepines on a long-term basis and with patients who have overdosed on barbiturates or tricyclic antidepressants.

Due to the short duration of flumazenil [60 min] compared to midazolam [2-6 hrs.] and other benzodiazepines, monitor closely for resedation for 2hrs. post flumazenil administration.

Procedure: <u>Preparation Phase</u>

<u>Assessing and preparing Your patient</u>

Assessing and preparing your patient reduces the risk of adverse outcomes and leads to improved patient satisfaction. Psychological assessment and preparation are important due to the anxiety associated with surgery or other invasive procedures that require sedation.

The psychological assessment should include the emotional state, ability to communicate, competency to provide an informed consent and cognitive understanding of the procedure and conscious sedation. Some exclusions to conscious sedation could be the developmentally disabled who usually require deeper sedation or general anesthesia to assure compliance with procedures.

Some physiological criteria that may exclude patients as good candidates for conscious sedation are those individuals with liver or kidney disease affecting the metabolism and excretion of the drugs used or patients with unstable arrhythmias or other situations requiring a more focused clinical situation.

A presedation assessment should be performed and documented to establish a baseline and to gain awareness of any factors that may increase the patients risk of complication from sedation/analgesia. This assessment may be performed by the physician or the nurse. The physician responsible for the procedure must review the presedation assessment before ordering sedative drugs.

The assessment should include the following:

(1) relevant medical/surgical history and current medications
(2) adverse or allergic drug reactions to anesthesia or sedation/analgesia
(3) history of tobacco, alcohol, or substance use or abuse
(4) timing and nature of last oral intake
(5) baseline mental status
(6) patient's weight, vital signs, and pregnancy status, if appropriate
(7) laboratory review and ECG (depending on institutional policy)

A written informed consent including the risks and benefits of sedation/analgesia will be documented and verified prior to procedure. After initial data collection and informed consent is obtained, an intravenous access line is established. This allows for the administration of sedation/analgesia and provides ready access for additional medications or IV fluids required during or after the procedure. EKG, NIBP (noninvasive blood pressure), and pulse oximetry monitors are applied and baseline vitals recorded. Equipment to administer supplemental oxygen should be present when sedation/analgesia is administered. If hypoxemia is anticipated or develops during sedation/analgesia, supplemental oxygen should be administered. When the patient's baseline oxygen saturation is <92 %, supplemental oxygen should be administered to keep oxygen saturation >92o throughout the procedure.

Procedure: <u>Administration Phase</u>

The patient will be monitored by a qualified individual whose primary responsibility is to monitor the sedated patient continuously throughout the entire procedure. The person evaluating the response of the patient to the drugs must NOT be the person performing the procedure. When monitoring a patient during conscious sedation, the goal is to maintain the patient relaxed, but arousable with protective reflexes intact.

Monitoring and documentation

- Vital signs, including blood pressure, heart rate,oxygen saturation and respiratory rate are observed and documented at a minimum of every 15 minutes and more frequently if patient condition warrants. Also observe these within three minutes of each additional dose of sedation/analgesia.
- Continuously monitor the level of consciousness. Using a sedation scale score, such as a Ramsay scale (see example), record finding with vital signs documentation every 15 minutes and PRN.
- Assess patient's pain tolerance every 15 minutes and PRN using pain rating scale.
- Observe and assess skin perfusion every 15 minutes and PRN.
- Detect and assess for adverse reactions such as emesis, respiratory distress, vasovagal reaction, diaphoresis or cardiorespiratory depression. Also be alert for hypovolemia, either caused by blood loss during the procedure or preexisting and unmasked by the sedative.
- Document time, dose, and route of all medications administered.
- Document type and amount of IV fluids infused, including blood product.
- Document untoward reactions or complications, as well as any interventions and subsequent patient response related to those events.

Post-procedure phase: Recovery period

The duration of the post-procedure recovery period may vary depending on the type and amount of sedative/analgesia administered, age, medical history and procedure performed.

- Monitor vitals, oxygen saturation and level of consciousness every 15 minutes until patient meets discharge criteria. EKG monitoring is included when indicated.

- Any patient receiving a drug antagonist (i.e., flumazenil, naloxone) shall have recovery monitoring for a minimum of two hours after administration and the patient is fully awake and alert. This time is necessary to ensure that the patient does not become resedated after reversal effects have abated.
- At no time should the sedated patient be left unattended.

Discharge criteria/aftercare instructions:

Vital signs, oxygen saturation and level of consciousness are stable compared to presedation baseline.

Patients requiring supplemental oxygen must meet pre-procedure baseline levels prior to discharge or transfer to a nonmonitored area.

Aldrete scoring system (example) or similar discharge criteria system may be used to determine readiness for discharge or transfer. The score range of "10" for complete recovery to "0" in comatose patients.

Patients may be discharged with score of "8" or above providing that activity, respiration, and color on the scale are scored at "2" and circulation and level of consciousness are scored at "1" or "2".

Complete written discharge instructions regarding post-procedure diet, medication, activity and phone number to use in case of emergency should be given to the ambulatory patient and/or responsible adult following recovery from sedation/analgesia. Outpatients should be discharged to a responsible **adult** who assumes responsibility for transport and is able to report any post-procedure complications.

Document and advise patient/family that following sedation/analgesia that the patient must not drink alcohol, drive an automobile, operate any dangerous machinery or undertake any responsible business matters for 24 hours. The qualified individual managing the patient during the recovery phase shall give report to the inpatient staff taking care of the patient.

ANTIPARKINSON DRUG - Entacapone

About 1-1/2 million Americans have Parkinson's disease, which is associated with a reduction in dopamine. A levodopa/carbidopa drug regimen is the most effective treatment, but its effectiveness often diminishes over time. Patients then fluctuate between periods of relatively good functioning ("on" periods or "on time") and periods of poor functioning ("off time").

Entacapone (Comtan, Novartis) is indicated as an adjunct to levodopa/carbidopa to treat patients who experience the end-of-dose "wearing off" phenomenon. Although the new drug has no antiparkinson effect of its own, it was associated with a significant increase in "on time" each day when added to the levodopa/carbidopa regimen in clinical trials.

In trials, entacapone caused no hepatotoxicity or liver enzyme elevation; significant advantage over tolcapone (Tasmar), a similar adjunctive drug that can cause severe hepatotoxicity. Because the addition of entacapone inhibits the metabolism and increases plasma concentrations of levodopa, patients may experience certain dopaminergic adverse events, such as dyskinesia and hyperkinesia, requiring a reduction in the levodopa dosage. Other commonly reported adverse effects include nausea, diarrhea, abdominal pain, and a brownish orange discoloration of the urine.

HYPNOTIC -- Zaleplon

Structurally unrelated to the benzodiazepines and other drugs prescribed to treat insomnia, zaleplon (Sonata, Wyeth-Ayerst) has a rapid onset of action and a short half-life. It's indicated for the short-term treatment of insomnia characterized by difficulty falling asleep. Because of its short duration of action, its effects are unlikely to persist more than four hours, it's not useful to treat insomnia characterized by early or frequent awakening.

The fast onset and short duration of action gives zaleplon an advantage over other hypnotics: It encourages the patient to try falling asleep on her own first. If she's unsuccessful, she can then take zaleplon without a risk of significant next-day sedation, a problem for other hypnotics taken after bedtime.

Zaleplon use should generally be limited to seven to ten days; the patient should be reevaluated if she's to take it for more than a few weeks. The usual dosage is 10 mg administered immediately before bedtime or after the patient has gone to bed and had difficulty falling asleep. A 20-mg dose has been satisfactorily tolerated in trials, although more adverse reactions may occur. Higher doses aren't recommended. A 5-mg dose may be indicated for elderly, debilitated, and underweight patients; those being treated with cimetidine; and those with mild to moderate hepatic impairment.

GASTROINTESTINAL DRUGS UPDATE

Metoclopramide look-alike:

Metoclopramide (Reglan), 10-mg tablets were once a round white tablet. The drug now is in a capsule-shaped pink tablet. The new capsule can easily be mistaken for metoprolol (Lopressor), 50 mg tablets which look very similar. Every nurse should be aware of the similarities in generic names .....

. .....Metoclopramide . metoprolol,

....and be aware of similar shape and size of the tablets. Reglan is used in the treatment of nausea and vomiting whereas, Lopressor is used to control hypertension and to reduce cardiovascular mortality after an acute MI.

OMEPRAZOLE (Prilosec Losec):

This drug is an anti-ulcer drug that is becoming more useful in treating severe esophagitis, and GERD (gastroesophageal reflux disease). This drug is administered orally in 20 to 80 mg in divided doses for a period of four to eight weeks therapy. This drug is not used for maintenance therapy. It is used for a specific length of time in order to allow the ulcer to heal (usually about four weeks).

OMEPRAZOLE may interact adversely with the following: ampicillin, iron derivatives, ketoconazole, diazepam, Dilantin, and warfarin. Adverse reactions to the drug include: headache, dizziness, diarrhea, nausea, vomiting, constipation, flatulence, rash, back pain, abdominal pain, and others. Be sure to have patient swallow these delayed-release capsules whole. Do not allow the patient to crush the capsule or to break open the capsules and swallow them.

U500 Insulin Update (ISMP, Jan 1997)

Eli Lilly Co. has just announced it is replacing purified pork U-500 insulin with human U-500 insulin. This concentrated form is for use in patients with marked insulin resistance who would otherwise need large volumes of insulin solution if U-100 were used. Since a U-500 syringe is not available, Lilly recommends that either a U-100 insulin syringe or a tuberculin syringe be used to measure doses. But when patients receive U-500 insulin with a U-100 insulin syringe, doses are sometimes miscommunicated by 5-fold. A patient using U-500 insulin with a U-100 syringe might state his dose as "40 units" when in reality he is reading "40 units" on the U-100 scale, but actually receiving 200 units.

SAFE PRACTICE RECOMMENDATION: Warning! Use extreme caution when expressing or interpreting doses of U-500 insulin. Consistent use of a tuberculin syringe with U-500 insulin is recommended, with total doses expressed in terms of both units and volume. For example, "200 units (0.4 mL)." Educate staff and patients about potential problems. Incorporate special quality assurance checks into preparation and handling of this drug in healthcare facilities. This product should also never be used intravenously because of the extremely serious nature of any inadvertent overdose.

INSULIN LISPRO, DNA-engineered alternative

Insulin lispro (Humalog, Lilly) is a human insulin analogue that's prepared using recombinant DNA technology. Insulin lispro is structurally similar to human insulin.

Indicated for patients with diabetes mellitus, insulin lispro may improve postprandial glycemic control by closely mimicking the body's natural rapid insulin output after a meal. And because it can be administered subcutaneously (S.C.) within 15 minutes before a meal, many patients should find taking it convenient. In contrast, regular insulin must be given between 30 minutes and one hour before meals to achieve optimal postprandial glycemic control.

One unit of insulin lispro lowers glucose as much as one unit of human regular insulin, but it has a faster onset of action and a shorter duration of action. Because of its brief duration of action, patients with Type I diabetes should also include a longer-acting insulin in their drug regimen.

Precautions: (1) Medications with hyperglycemic activity (for example, corticosteroids) may increase insulin requirements; closely monitor blood glucose concentrations when one of these drugs is used concurrently with insulin lispro. (2) The risk of hypoglycemia is increased by the concurrent use of other medications that can lower blood glucose concentrations (for example, oral hypoglycemic agents and salicylates).

Adverse reactions: hypoglycemia, allergic reactions, injection-site reactions
Supplied as: 10-ml vials and 1.5-ml cartridges containing 100 units/ml

Dosage: individualized for each patient and administered S.C. immediately after mixing and within 15 minutes before a meal

Nursing considerations: (1) Store the vials or cartridges in a refrigerator. (2) When insulin lispro is mixed with Humulin N, the rate of absorption decreases, but bioavailability doesn't. The absorption rate isn't decreased when insulin lispro is mixed with Humulin U. (3) When you mix insulin lispro with a longer-acting insulin, draw the insulin lispro into the syringe first to prevent clouding of the insulin lispro by the longer-acting insulin. (4) Teach all patients with diabetes to regularly monitor their blood glucose concentrations at home with blood glucose meters. (5) There have been numerous reports of patients confusing Humalog (insulin lispro) with Humulin R (regular human insulin). Warn patients about the similar names. (6) Closely monitor pregnant women and nursing mothers who are using insulin lispro. (7) Beta-adrenergic blocking agents (for example, propranolol) may mask the symptoms of hypoglycemia in some patients. (8) Teach your patient about the signs and symptoms of hypoglycemia and how to treat the condition.

Rosiglitazone maleate

Improving insulin sensitivity Rosiglitazone maleate (Avandia, SmithKline Beecham; Bristol-Myers Squibb) is indicated as monotherapy (as an adjunct to diet and exercise) and in combination with metformin to control Type 2 diabetes mellitus. Like troglitazone and pioglitazone, the two other thiazolidinedione antidiabetic drugs on the market, rosiglitazone increases sensitivity to insulin in muscle and adipose tissue and decreases hepatic glucose output. It depends on the presence of insulin for activity, but doesn't stimulate insulin secretion.

In clinical trials, rosiglitazone didn't cause liver problems. But because the related drug troglitazone has been associated with idiosyncratic hepatotoxicity (resulting in a few cases of liver failure, liver transplants, and death), clinicians need to be aware of the potential for adverse liver effects. Serum alanine aminotransferase (ALT) concentrations should be checked and therapy withheld if the baseline value is more than two and a-half times the upper limit of normal (ULN). After therapy starts, monitor ALT values every two months for the first 12 months and periodically thereafter. Discontinue therapy if ALT concentrations persistently exceed three times the ULN or if the patient is jaundiced.

Consult the product literature for more specific guidelines and precautions. Rosiglitazone has been associated with cholesterol increases and weight gain. Research data suggest that it's less likely than the other two thiazolidinediones to interact with other drugs.

Precautions: (1) Should not be used in patients with Type 1 diabetes and those experiencing diabetic ketoacidosis. (2) Should not be used in patients with New York Heart Association class III or IV cardiac status unless expected benefits outweigh the risks because thiazolidinediones may cause plasma volume expansion, increasing cardiac preload. (3) Don't initiate treatment if the patient exhibits evidence of active liver disease according to product guidelines. Throughout therapy, monitor the patient for signs of drug-induced hepatotoxicity according to product guidelines. (4) Use caution in patients with edema: Mild to moderate edema has been reported with use of rosiglitazone.

Adverse reactions: upper respiratory tract infection, injury, headache, edema, anemia. Supplied as: tablets containing the equivalent of 2 mg, 4 mg, and 8 mg of rosiglitazone. Dosage: Initially, 4 mg/day as a single dose in the morning or as a divided dose taken in the morning and evening. If indicated after 12 weeks of treatment, dosage may be increased to 8 mg/day as single or twice-daily divided dose.

Nursing considerations: (1) Instruct the patient to report any signs and symptoms of hepatic dysfunction, such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, and dark urine. (2) Teach the patient how to monitor his blood glucose and recognize and treat hypoglycemia. Although thiazolidinediones aren't likely to cause hypoglycemia when used alone, combining them with other antidiabetic drugs increases the risk; dosage adjustments may be indicated. (3) Inform women of childbearing potential that improved insulin sensitivity may allow ovulation to resume, increasing the risk of pregnancy. Advise them to use adequate contraception. (4) Tell the patient that rosiglitazone may be taken without regard to food. (5) A 1-week washout period is recommended when rosiglitazone is initiated in a patient who was previously taking troglitazone. (6) Renal excretion of rosiglitazone is negligible, so dosage adjustments aren't necessary for patients with impaired renal function.

Miglitol ,

Joining acarbose, miglitol (Glyset, Pharmacia & Upjohn) is the second alpha-glucosidase inhibitor to be marketed. It acts locally by inhibiting alpha-glucosidases (such as sucrase and maltase) in the small intestine.

By delaying the digestion and absorption of ingested carbohydrates, miglitol limits the rise in blood glucose concentrations following meals. Systemic absorption of the drug apparently doesn't contribute to this therapeutic effect. Fermentation of undigested carbohydrates accounts for the adverse gastrointestinal (GI) effects (pain, gas, and diarrhea) associated with the drug. In trials, the incidence of these effects diminished with continued use.

Miglitol is indicated as an adjunct to diet for patients with Type 2 diabetes mellitus whose hyperglycemia can't be managed with diet alone. It may also be combined with a sulfonylurea for additive effects. Unlike acarbose, miglitol hasn't been associated with elevated liver enzymes or jaundice, so liver function needn't be monitored during therapy--an advantage for miglitol.

Miglitol is excreted primarily by the kidneys and may accumulate in patients with renal problems. However, because its therapeutic effect occurs locally, reducing the dosage for these patients would decrease the therapeutic effect. Consequently, miglitol isn't appropriate for patients with significant renal impairment.

Precautions: (1) Contraindicated for patients with inflammatory bowel disease, colonic ulceration, and partial intestinal obstruction and for patients predisposed to intestinal obstruction. (2) Contraindicated for patients with chronic GI diseases associated with marked disorders of digestion or absorption or with conditions that may be exacerbated by increased gas formation in the intestine. (3) Don't use miglitol concurrently with intestinal adsorbents, such as charcoal, or digestive enzyme preparations containing carbohydrate-splitting enzymes, such as amylase or pancreatin. (4) Not recommended for patients with significant renal dysfunction (serum creatinine greater than 2 mg/dl). (5) Miglitol may affect the bioavailability or plasma concentrations of certain drugs, such as ranitidine, propranolol (Inderal), and digoxin. Consult the product literature for a complete listing of potential drug interactions. (6) Use caution if the patient is taking miglitol concurrently with medications such as thiazide diuretics and corticosteroids known to increase blood glucose concentrations.

Adverse reactions: abdominal pain, diarrhea, flatulence, skin rash, low serum iron concentrations. Supplied as: tablets at 25-mg, 50-mg, and 100-mg potencies. Dosage: Initially, 25 mg three times daily (at the start of each meal) for 4 to 8 weeks; if indicated, dosage may then be increased to 50 mg three times daily. If the patient's response isn't adequate after about 3 months at this dosage, it may be increased to 100 mg three times daily (the maximum recommended dosage).

Nursing considerations:

(1) Some patients may benefit from a starting dosage of 25 mg just once a day to minimize GI effects; the frequency can be gradually increased to three times a day.
(2) Teach the patient to take miglitol with the first bite of each main meal. Explain that the low starting dosage will help minimize adverse GI effects.
(3) Teach the patient how to monitor his blood glucose and to recognize and treat signs and symptoms of hypoglycemia, which may occur when miglitol is used in combination with other antidiabetic drugs.
(4) Instruct him to treat mild-to-moderate hypoglycemia with oral glucose (dextrose)--not sucrose (or table sugar) because miglitol inhibits its conversion to glucose. Tell him to have a source of glucose readily available at all times.
(5) Treat severe hypoglycemia with parenteral glucose or glucagon injection.

Anti-obesity Drua: Orlistat

Orlistat works by blocking fats in the GI tract. Unlike most drugs prescribed for weight control, orlistat (Xenical, Roche) isn't an appetite suppressant. Instead, it helps reduce calorie intake by inhibiting the digestion of triglycerides in the GI tract. Taken in the recommended dosage, orlistat reduces the absorption of dietary fat by approximately 300.

Used in conjunction with a reduced-calorie diet, orlistat is indicated for obesity management (weight loss and weight management) and to reduce the risk of regaining weight after prior weight loss. Initiating therapy is considered appropriate for obese patients with a body mass index (BMI) of 30 kg/m2 or higher, or 27 kg/m2 or higher in the presence of other risk factors, such as hypertension, diabetes, or dyslipidemia. (BMI is calculated by dividing weight in kilograms by height in meters squared.)

Problems associated with orlistat are related to its effect in the GI tract (systemic absorption is minimal). Most adverse GI effects are mild and transient, but the likelihood increases if the patient's diet is high in fat. A nutritionally balanced, reduced-calorie diet that provides about 30s of calories from fat should be part of the treatment regimen.

Precautions:

(1) Contraindicated in patients with chronic malabsorption syndrome or cholestasis. (2) Use cautiously in patients with a history of hyperoxaluria or calcium oxalate nephrolithiasis because the drug may cause increased concentrations of urinary oxalate.

(3) Closely monitor coagulation parameters in patients taking warfarin because orlistat may reduce absorption of vitamin K.

(4) Reduced dietary intake associated with orlistat therapy may affect the absorption of cyclosporine.

Adverse reactions: oily spotting from rectum, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation, fecal incontinence.

Supplied as: 120-mg capsules
Dosage: 120 mg three times a day with each main meal containing fat

Nursing considerations:

(1) Tell the patient to take a capsule with each main meal containing fat (during or up to one hour after the meal). If he misses a meal or the meal contains no fat, he should omit the dose.

(2) Because orlistat may reduce absorption of vitamins A, D, E, and beta-carotene, tell the patient to take a daily multivitamin supplement. To ensure efficient absorption, he should take the supplement at least two hours before or after the administration of orlistat (such as at bedtime).

(3) Advise him to stick to a low-fat diet, as prescribed. Inform him that the risk of adverse GI effects increases when orlistat is taken with high-fat meals.

(4) Be aware that orlistat's trade name, Xenical, has been confused with Xeloda, the trade name for the antineoplastic drug capecitabine. Carefully follow standard drug administration precautions to avoid misinterpreting an order.

ANTISECRETORY DRUG – Rabeprazole sodium

Rabeprazole sodium (Aciphex, Eisai, Janssen) is the third proton pump inhibitor to be marketed in the United States, joining omeprazole (Prilosec) and lansoprazole (Prevacid). These drugs inhibit the gastric enzyme system known as the acid or proton pump, blocking the final step of acid production. It's currently labeled for four indications:

- **short-term (up to 4 weeks)** treatment and symptom relief of duodenal ulcers
- **short-term (up to 8 weeks)** treatment and symptom relief of erosiveor ulcerative gastroesophageal reflux disease (GERD) maintenance treatment and heartburn reduction in patients with erosive or ulcerative GERD
- **long-term treatment** of hypersecretory conditions, including Zollinger-Ellison disease.

RESEARCHING NEW DRUGS

This page is a guide to the research of new drugs. Each nurse has the responsibility to safely administer medications. Therefore, it is imperative that you research new drugs and/or drugs that are unfamiliar to you. Use the following outline to determine if you are ready to safely administer a new drug. If you do not know each of the items on this outline, you need to research the drug further.

FACT	BEHAVIOR
1. Action of the drug and expected outcome of drug therapy	a. (pathophysiology) *observe patient for signs of drug action as expected
	b. state how the drug works and the expected outcome for the patient
2. Mechanics of the Administration of the drug	a. what routes can be used
	b. differences in effect of the drug when given by different route
	c. preparing drug for administration
	d. factors affecting absorption
3. Adverse Reactions	a. observe for expected side effects
	b. be prepared to intervene if severe side effects occur
4. Drug Interactions	a. review patient history for allergy, medical problems, surgeries (any other contraindications)
	b. review patient's medication profile for interactions that could be harmful

This was a guide to use before administering new medications. It's use demonstrates a thorough knowledge of the drug and the pathophysiology connected with its use. Many reference sources exist that can give you all information needed to answer all the above questions. Consult hospital pharmacist if still in doubt about a medication.

Psychotropic Drugs Update:

This group of drugs covers a wide variety of different drugs. We use the term "psychotropic" to mean ALL DRUGS that affect the mind. "Psychotropic Drugs" include the mild drugs used to treat anxiety; and it includes the major tranquilizers used to treat SEVERE psychosis. It also includes all drugs in between these two extremes. For example: anti-anxiety drugs; anti-depressants, hypnotics, anti-psychotics, sedatives, tranquilizers, bipolar drugs, psychostimulants, and others.

In this text, we will not be presenting ALL of the above categories of drugs. We do not have enough space in this course. We will be including the following categories of drugs and the newest drugs in these categories. As you review these newer drugs and drug therapies, keep in mind that drug therapy is just a part of the overall therapy for the patient. Also remember that these drugs are very powerful and may have severe side effects. Always be alert for any adverse reactions to these drugs.

Before administering any of these potent drugs, the nurse should be familiar with the medical and psychiatric history of the patient. The nurse should also perform a complete physical exam on the patient; or have access to the physical exam results obtained by the patient's doctor or other nursing staff members. The nurse must be aware of any medical problems the patient may have, including, but not limited to the following: past or present cardiovascular disease; liver disease; kidney disease; seizure disorders; current medication use; and any allergies.

Psycho-tropic Drugs Update

A Antidepressants

1. Desyrel (trazodone) is from a class of newer antidepressants. It has been found to effectively treat the symptoms of clinical depression.

SIDE EFFECTS: drowsiness, dizziness, dry mouth, nausea, headache, priapism

- drowsiness--this is a common problem with Desyrel; many people are instructed to take this drug at bedtime due to the persistent drowsi ness.
- priapism--In rare cases, Desyrel has been reported to cause this disorder which is painful erection that persists even in the absence of sexual stimulation; it may lead to impotence and/or gangrene of the penis.

2. Effexor (venlafaxine) ....is a fairly new antidepressant that is thought to have the therapeutic effects of SSRI's and TCA's combined. For some people, Effexor relieves the symptoms of depression better than other medications, perhaps because it increases the levels of both serotonin and norepinephrine (two neurotransmitters thought to cause the symptoms of depression) in the brain.

SIDE EFFECTS: headache, nausea, sexual difficulties, weight loss

Rare side effects:

- anxiety, nervousness, blurry vision, diarrhea, dizziness, dry mouth, insomnia
- hypomania

3. Remeron (mirtazapine) ....

Remeron is a new medication which may relieve the symptoms of depression better than SSRI's or TCA's. Though Remeron has only been available in the United States since June 1996, it is thought to be particularly useful in reducing anxiety and sleep problems which often accompany depression. Researchers continue to investigate the effectiveness of Remeron.

SIDE EFFECTS: dizziness, drowsiness, weight gain, dry mouth, constipation

Rare side effects/risks: agranulocytosis, hypomania

4. Serzone (nefazodone)...

Serzone is a newer antidepressant which has relieved the symptoms of depression in many patients who were not helped by **SSRI's** or TCA's. Serzone may improve sleep quality better than other antidepressants and often decreases the troublesome side effect of sexual dysfunction.

SIDE EFFECTS: drowsiness, dry mouth, nausea, dizziness, blurred vision

Additional side effects/cautions: weakness, hypomania, priapism

5. Wellbutrin (bupropion)...

Is a relatively new medication that is used to treat depression and recently, has been found to relieve the symptoms of ADHD, ***Attention Deficit Hyperactivity Disorder*** for some people. Wellbutrin works by altering the communication between nerve cells, or neurons, in the brain. Wellbutrin has been found to be particularly effective for adolescents and adults who were diagnosed as "hyperactive" or "autistic" as children. Many of these children exhibit mild to severe depression when they become young adults and Wellbutrin has shown to be especially effective to treat depression in these adults. Wellbutrin may be used alone or in combination with other antidepressants such as prozac or trazadone.

SIDE EFFECTS: weight loss, agitation, constipation, dry mouth, headache

less common side effects:

- insomnia, nausea, skin problems, tremors
- hypomania, seizures

Antidepressants (continued) SSRI Antidepressants

SSRI's are newer antidepressants which often treat the symptoms of depression more effectively than TCA's and for many people, produce fewer troublesome side effects. Besides treating depression, these drugs are sometimes used to treat the symptoms of obsessive-compulsive disorder. Luvox in particular, is thought to help patients control their obsessions and compulsions.

The following **SSRI** medications have common side effects listed below:

- Prozac (fluoxetine
- Zoloft (sertraline)
- Paxil (paroxetine)
- Luvox (fluvoxamine maleate)

SIDE EFFECTS: headache, nausea, sexual difficulties, weight loss

occasional side effects:

- anxiety, nervousness, diarrhea, dizziness
- dry mouth, insomnia
- hypomania

TCA Antidepressants Tricyclic Antidepressants

The tricyclic antidepressants were one of the first classes of antidepressants developed. Though they do generally have more side effects than the SSRI's some people find them more effective in treating the symptoms of clinical depression.

These drugs have been used since 1958, when they were accidentally discovered to have antidepressant properties. These agents do not generally produce CNS stimulation or euphoria like the MAO inhibitors. They will usually produce mood elevation with increased mental alertness and physical activity within a few days of administration. They also have a mild sedative effect which makes them ideal for treating depression associated with anxiety. Adverse effects include anticholinergic effects of dry mouth, blurred vision, and others: hypotension, tachycardia, some cardiac arrhythmias, and occasional allergic reactions such as skin rashes and photosensitivity.

The tricyclic group is thought to act by increasing the concentration of available neurotransmitters at the receptor sites via inhibition of the reuptake of norepinephrine or serotonin. They are the drugs of choice in the treatment of endogenous depression, providing relief from the overwhelming feelings of sadness loneliness, fatigue, isolation, anxiety, and hopelessness. In addition, the tricyclics are beneficial in treating such symptoms as insomnia, early morning wakening, anorexia, and loss of libido. These drugs are used successfully about 850 of the time.

Following is the current list of TCA's:

- Amitriptyline; (Elavil, Endep) **usual dose: 50-100mg per day**
- Amoxapine; (Asendin) **usual dose: 50-400mg per day**
- Clomipramine; (Anafranil)
- Desipramine; (Norpramine, Pertofrane) **usual dosage: 75-150mg per day**
- Doxepin; (sinequan, Adapin) **usual dose: 50-100mg per day**
- Imipramine; (Tofranil, Antipress, Imavate, Janimine, SK-Pramine) **usual dose: 50-150mg per day**
- Maprotiline; (tetrocyclic, Ludiomil) **usual dose: 75-300mg per day**
- Nortryptyline; (Pamelor, Aventyl) **usual dose: 20-100mg per day**
- Protriptyline; (Vivactil) **usual dose: 10-40mg per day**
- Trimipramine; (Surmontil) **usual dose: 50-100mg per day**

Side Effects common to the TCA's:

- constipation, weight gain, diarrhea, nausea,
- dizziness, drowsiness, dry mouth, headache,
- anxiety, nervousness, blurry vision, insomnia, tremors
- sexual difficulties, urinary retention,
- rarely: heart arrhythmias, hypomania, liver irritation, seizures

Nursing considerations: Tricyclic Antidepressants

1. Maximum antidepressant effects generally appear within 2-3 weeks. If no therapeutic response is observed after 4-8 weeks, the drug is usually discontinued and another substituted.

2. Patients advised to report fever, malaise, sore throat, or sore mouth, which are early signs of agranulocytosis. Patient should be placed in protective isolation pending results of blood evaluation.

3. Check for abdominal distension, which may result from urinary retention or constipation.

4. High dose increases the frequency of seizures in epileptic patients and may cause eliptiform seizures in normal individuals.

MAOI, Monoamine Oxidase inhibitors

MAOI's are of two major chemical types, the hydrazides and nonhydrazides. Their actions are said to be from their ability to inhibit the MAO, thereby, increasing the brain concentrations of norepinephrine and serotonin and also producing central nervous system stimulation. The MAO inhibitors are generally less effective than the other group of drugs, the tricyclics. The MAO inhibitors are also more toxic to the body. In most cases, they are used only when other types of antidepressants fail to work for specific patients.

MAOI's are usually contraindicated in asthma, cerebral vascular disease, congestive heart failure, hypertension, hypernatremia, impaired kidney function, cardiac arrhythmias, pheochromocytoma, hyperthyroidism, liver disease, severe headaches, alcoholism, glaucoma, atonic colitis, paranoid schizophrenia, debilitated patients, patients over age 60, pregnancy, and in children under 16 years old.

Adverse effects include: orthostatic hypotension, nervousness, insomnia, in high doses, tremors, and convulsions. Hepatotoxicity and blood dyscrasias may occur. Certain drugs in this class have also been reported to produce: severe headaches and fatal hypertensive crises.

hypertensive crisis develops as a result of ingesting certain types of foods. Patients are warned not to eat foods that are rich in tyramine. The person taking MAO inhibitors must avoid these foods or it can lead to death by hypertensive crises. The foods include:

- aged cheeses (cheddar, Camembert, Gruyer), (cream cheese and cottage cheeses are acceptable)
- alcohol; wines (especially Chianti), and beer are the worst
- beef or chicken liver
- pickled fish (herring), pickled poultry, pickled meats
- smoked fish, soy sauces
- broad beans (fava beans and others)
- bananas, raisins, tomatoes
- avocados, spinach
- caffeinated beverages
- orange pulp, yogurt
- certain packaged soups

As you can see the list of contraindications and adverse effects is very long. This is for good reason. These drugs are powerful and can have serious side effects. Always be on the alert to any adverse symptoms when patients are taking these drugs. Always teach patients to contact their doctor immediately if they experience any (even mild) side effects.

a. Isocarboxazid, (Marplan)

b. Phenelzine, (Nardil)

*these two drugs above have slow onset of action; 2-4 weeks; high incidence of adverse reactions;

usual dosage of both: PO: 15-30 mg/day

c. Tranylcypromine, (Parnate)--nonhydrazide group; produces CNS stimulation; faster onset of action than above drugs; is clinically more effective than above drugs with fewer adverse reactions; usual dosage: PO: 20-30 mg/day

**Reminder- -these drugs may have very severe side effects. Always have patients report any and all side effects.

Nursing considerations: Monoamine Oxidase Inhibitors

1. Maximum antidepressant effects may require 2-6 weeks. If no beneficial effects occur after 3-4 weeks, the MAGI is usually discontinued and another drug substituted.

2. Ingestion of foods containing tyramine can cause a severe hypertensive reaction. Provide the patient or responsible family member with a list of foods and beverages to be avoided during therapy and for 2-3 weeks after therapy is discontinued. Excessive use of beverages with caffeine may increase risk of hypertensive reaction.

3. Instruct the patient to immediately report any headache or palpitations, symptoms which may indicate an impending hypertensive crisis.

4. Caution the patient to avoid overexertion because these drugs may suppress anginal pain, which serves as a warning of myocardial ischemia.

5. Patients receiving prolonged therapy may develop optic damage. Changes in red-green vision may be the first indication and should be checked periodically.

6. Medication for treatment of drug overdose should be readily available; phenothiazine antipsychotic agents for agitation, etc.

B MOOD STABILIZERS

1. Depakote (sodium divalproex)...

Depakote is effective in decreasing depressive and manic episodes among people with bipolar disorder. It is often prescribed to people if lithium and Tegretol were unsuccessful in relieving the symptoms of bipolar disorder.

SIDE EFFECTS:

- ***Most common side effects--drowsiness and nausea***
- Less common side effects: constipation, diarrhea, weight gain,
- anxiety, dizziness, hair loss, headache, tremors,
- liver irritation, pancreas problems

2. Lithium

Lithium Carbonate is a special class, it is a mineral salt with special properties. Given to normal persons, there is no effect from this drug. Lithium carbonate (Eskalith, Lithonate, Lithane) dosage is adjusted by sampling blood levels in the patient. 300 mg TID or QID is about average. This drug will help to reduce the great mood swings present in the manicdepressive disorder. Full effect is seen in about 7 to 10 days of therapy. Lithium is usually administered along with an antipsychotic agent during the time it takes for peak blood levels to be realized.

The adverse effects include:

- fatigue, slurred speech, muscle weakness, and tremors
- Toxic doses cause muscle rigidity, convulsions and coma.

The problem with management of this drug is critical. Therapeutic dose of this drug is very close to toxic levels. Blood levels must be monitored carefully until the patient is stable. Diet must be watched carefully, especially fluid intake.

3. Tegretol (carbamazepine)...

Carbamazepine (Tegretol), an anticonvulsant drug used for the treatment of psychomotor and grand mal seizures and trigeminal neuralgia, has more recently emerged as an agent to be used in psychiatric treatment. In animal studies, this drug has been shown to be effective in inhibiting the kindling phenomenon in the limbic system and temporal lobe region. Kindling can be " ....described as repeated subthreshold electrical stimulation that culminates in the development of major motor seizures or psychopathology."

As a result of this inhibition of kindling, Carbamazepine has been reported to be useful in affective disorders, especially bipolar disorders, decreasing symptoms, and demonstrating some antidepressant effect. The reduction of symptomatic behavior in clients with aggression, dyscontrol syndromes, and schizophrenia has also been reported.

Therapeutic levels of carbamazepine, like lithium, are evaluated based on symptom control and periodic serum level determinations. This drug also has a high potential for toxicity. Carbamazepine is useful alone or with lithium in the treatment of bipolar affective disorder, especially if a client is intolerant or unresponsive to lithium.

C ADHD Medications:

1. Adderall...and other stimulant drugs:

Adderall is a drug containing mixed salts of a single-entity amphetamine product. This drug typically improves attention span and the ability to concentrate in ADHD.

Additional stimulant drugs:

Cylert (magnesium pemoline)
Dexedrine (dextroamphetamine)
DextroStat (dextroamphetamine sulfate)
Ritalin (methylphenidate)

Stimulants are sometimes used to treat depression, especially among people who experience unpleasant side effects from standard antidepressants such as TCA's and MAOI's.

Stimulants are also used to treat narcolepsy, a sleep disorder characterized by sudden and unpredictable sleep attacks.

SIDE EFFECTS:

- loss of appetite, weight loss, insomnia, headache
- tics, dizziness, irritability, stomach pain, tachycardia, hallucinations

2. Catapres (clonidine) ....is an antihypertensive and an alternative to stimulants for treating ADHD. It seems to work best in decreasing hyperactivity, but does not always improve distractibility, (as stimulants do). Some physicians have found benefits in using this medication with children who have ADHD and conduct problems.

***Tenex (guanfacine)** is another drug that has been reported to effectively treat the symptoms of ADHD.

SIDE EFFECTS:

- constipation, dizziness, drowsiness, dry eyes, dry mouth, nausea, sexual difficulties, skin problems
- less common: anxiety, depression, insomnia, nightmares, urinary retention, hallucinations

Nursing Considerations: Antidepressants and Lithium

1. Preparation and education of family & patient is essential in order to promote patient compliance. Information to be included should be the nature of depressive illness; that approximately 2-3 weeks of drug therapy are required for clinical improvement to be seen; that the drug must be taken precisely as prescribed; the return appointment must be kept in order to evaluate effectiveness of the therapy. 2. Monitor pulse and blood pressure when therapy is initiated and at regular intervals thereafter. To avoid hypotensive reactions, instruct patient to make changes in position slowly, avoid standing in place for long periods of time, and avoid hot baths or showers, which cause vasodilation.
3. Advise the patient to avoid the use of any other prescription or nonprescription drugs or alcohol while taking antidepressant drugs and for 2-3 weeks after discontinuing them, without first consulting their physician.
4. MAO inhibitors and tricyclic antidepressants should usually not be administered together without the expresses consent of the physician, who should be fully apprized of the potential dangers of this combination. At least 10 days should elapse between discontinuing MAOI therapy and initiating the use of tricyclics.
5. Observe the patient closely for indications of contemplated suicide. Patients receiving these drugs are most prone to attempt suicide when the response to therapy begins and after they emerge from the depths of depression.
6. Observe diabetic patients for potential loss of control of blood sugar. MAOI drugs potentiate the hypoglycemic effects of insulin and oral agents; reduced dosage may be necessary. Tricyclics may produce hypoglycemia or hyperglycemia in some patients.

Nursing Implications for the Antidepressants (Nursing96)

Approximately 5% of people in the U.S. suffer from depression that requires medical attention and/or drug therapy. Therefore, you may expect to care for a number of patients with clinical depression in your nursing career. Although the antidepressant medications significantly improve serious depression, the nurse must be aware of those patients who still exhibit signs and symptoms of depression while hospitalized for other medical or surgical problems.

Patient Teaching considerations:

1. Antidepressants are safe and effective.

Working naturally in the brain, they usually are not addictive and generally are safe when taken as prescribed. Don't confuse antidepressants with tranquilizers or with pain killers. An antidepressant will not numb your body, mind, or emotions, as many people think. Rather they will make you more perceptive and aware of your feelings, helping you deal more effectively with the pain and suffering depression causes.

2. People respond to antidepressants differently.

Although some patients notice an improvement within days of starting treatment, others don't experience maximum benefits for up to eight weeks. Most people see an improvement within two to four weeks. If you don't initially respond to therapy, don't worry--the benefits of treatment will be worth the wait. But if you believe your antidepressant isn't working after a fair trial, consult your physician. He may prescribe another medication.

Because people may respond differently to the same drug, what works well for someone else may not work at all for you. Keep in mind that several different classes of antidepressants are available. During initial treatment, you may need to consult with your physician and try a different antidepressant and dosage.

The same is true for side effects. One antidepressant may work well for you but cause side effects; and another antidepressant may work just as well without unwanted side effects.

3. Most people who take antidepressants experience few, if any, side effects

Although most side effects are mild and disappear within two to three weeks of starting treatment, notify your physician of all reactions you experience, especially if one is particularly troublesome, such as blurred vision. Don't wait for your next appointment.

Don't take any additional drugs without first checking with your physician. When antidepressants are taken alone, they are relatively harmless, but when taken with certain other drugs, they can become dangerous.

Keep in mind that being depressed is usually more unhealthy than the side effects caused by medications. Some people find that their side effects seem minimal compared with the positive results they get from antidepressant therapy.

4. Antidepressant therapy will help you return to a normal sleep cycle.

Insomnia is a common complication of depression, and getting a good night's sleep is a significant part of the healing process. If you have trouble sleeping after you have been taking an antidepressant for a while, inform your physician. You could be experiencing medication-induced insomnia.

To alleviate insomnia, your physician may prescribe one antidepressant for you to take early in the day and another antidepressant--one that causes drowsiness--at bedtime. But remember, the drowsiness is just an effect of that particular drug--antidepressants aren't sleeping pills or sedatives.

Teach your patient about antidepressants and help him see that the benefits of his medication will far outweigh the drawbacks.

D Antianxiety Medications

The general action of this class of drugs is said to be from their action on the subcortical sites and depression of the limbic system. In very high doses or overdoses, depression of the cerebral cortex can occur, the result being a sedative effect. Most drugs in this category also have anticonvulsant activity, skeletal muscle relaxant effects, and effects on the central nervous system as mentioned above.

Most of these drugs are usually administered in the daytime in order to control moderate to severe anxiety and tension in patients with neuroses and mild depressive states. Recently, they have been indicated for those who suffer from the excessive environmental stress syndrome. Each of the drugs we will mention, may have some other specific effects and actions. However, we will still classify these drugs into broad categories.

1. BuSpar (buspirone) .....

BuSpar is often prescribed to people with generalized anxiety disorder to relieve anxiety and agitation. Also, BuSpar is sometimes prescribed with Prozac to treat the symptoms of depression or obsessive-compulsive disorder. For some people, BuSpar is a good alternative to benzodiapines since it does not act as a sleep agent like other antianxiety medications. However, it takes about two to four weeks to see the full effects of BuSpar, whereas benzodiapines begin working almost immediately.

SIDE EFFECTS:

- dizziness, headache, nausea
- insomnia

Benzodiazepine---Antianxiety Medications

Benzodiazepines, also called antianxiety drugs or minor tranquilizers, are used to facilitate sleep, relieve anxiety, or decrease agitation. Sometimes, benzodiazepines are used to alleviate the symptoms of bipolar disorder, panic attacks, or phobias. Since they begin working within a few hours after the first dose is taken, benzodiazepines provide relief to many people. However, they are usually only prescribed for a short time, due to severe withdrawal symptoms which are sometimes experienced when the medication is taken at high doses for a long time or discontinued abruptly.

General side effect of these are:

- drowsiness, ataxia, and muscle weakness
- atropine-like side effects; dry mouth, blurred vision, etc.
- impairment of sexual functions, menstrual irregularities.

Benzodiaze-Dine Derivatives---

These drugs work by potentiation of gamma-aminobutyrate (GABA). They are also indicated for use in insomnia, alcohol withdrawal, panic attacks, generalized anxiety disorder, and seizure disorders. Elderly patients and patients with medical conditions may require lower doses. CNS depressants increase sedation with these drugs. Alcohol, disulfiram, valproic acid, and isoniazid all lower the metabolism of the benzodiazepines. Estrogens and rifampin increase the metabolism of the benzodiazepines. Antacids lower absorption of these drugs. Alcohol increases absorption of these drugs.

1. Chlordiazepoxide, (A-poxide, Librium, Sereen, Murcil)

This drug is used as an anti-anxiety drug, for withdrawal from alcohol, and to relieve pre-op anxiety and tension. This drug is usually less potent than others in this class. The intravenous form is to be used immediately after reconstitution. The usual dosage; depends upon the use: PO: 5-25 mg 3-4 times a day, IM or IV: 50-100 mg up to a maximum of 300 mg. child over six: 5 to 10 mg 2-3 times in 24 hours.

2. Clorazepate dipotassium, (Tranxene, Tranxene-SD, Azene)

This drug is used as an anti-anxiety drug and for alcohol withdrawal. It is not recommended for use in those under the age of 18 years. The usual dosage: PO: 15-60 mg at h.s. or in 2-4 divided doses.

3. Diazepam, (Valium, Valrelease)

This drug is perhaps the most widely prescribed drug in this class of drugs. Perhaps it is the most widely prescribed drug in the U.S. It i8 used as an anti-anxiety drug, for tension, pre-op anxiety, acute alcohol withdrawal, anticonvulsant, in conjunction with certain anesthesias, and many other similar uses. Usual dosage: PO: 2-5mg 2-4 times a day IV: 2-10 mg repeat 3-4 hours PRN. These are some of the others in this category. They have the same general actions, uses, and side effects:

- Halazepam (Paxipam)
- Lorazepam (Ativan)
- Oxazepam (Serax)
- Prazepam (Centrax)
- Alprazolam (Xanax)
- Flurazepam (Dalmane)
- Quazepam (Doral)
- Temazepam (Restoril)
- Triazolam (Halcion)
- Clonazepam (Klonopin)
- Estazolam (ProSom)
- Midazolam (Versed)

E Non-Benzodiazepine Anti-Anxiety Drugs:

1. Meprobamate, (Bamate, Equanil, Miltown, Mepriam, F.M.-400)

This drug is commonly used for anti-anxiety, tension, insomnia in anxious and tense patients, and as an adjunct in the treatment of tetanus. It is generally more potent than the Benzodiazepine derivative drugs.

The drug must be withdrawn slowly. The usual dosage: PO or IM, 400mg 34 times daily. This drug is also highly abused and is prescribed sparingly. Side effects: drowsiness, ataxia, atropine-like side effects. Toxic effects: lethargy, stupor, coma, shock, cardio-respiratory failure.

2. Tybamate, Tybatran

This drug is used as an anti-anxiety drug, for tension, for the control of agitation in the elderly, and as adjunctive therapy in psychotic states. This drug is similar to Meprobamate (above). However, this drug usually has less sedation and fewer side effects than Meprobamate. The usual dosage: P0: 250-500mg, 3-4 times daily.

3. Chlormezanone, Trancopal

This drug is used as an anti-anxiety drug and for relief of tension. It has the same general actions of the diazepam group. This drug is generally less effective than diazepam and has few side effects. Usual dosage is PO: 100500mg 3-4 times daily; children: PO: 50-100mg 3-4 times/day.

4. Hydroxyzine HC1, Atarax and **Hydroxyzine pamoate,** Vistaril

These drugs are very similar in action. They are used as anti-anxiety drugs and for tension. They are also used as antihistamines, local anesthetics, for acute alcohol withdrawal, antiemetics, pre-op and post-op adjunctive therapy, and Vistaril is commonly used as an adjunct with

narcotic analgesics to enhance their effect.

Atarax: PO 25-100 mg 3-4 times daily
Vistaril: IM: 50-100 mg child: 25-100 mg IM

adverse effects: drowsiness, atropine-like effects, dry mouth, blurred vision

The previous drugs are mainly used for mild anxiety-related problems and/or insomnia. Most drugs in this category have mild side effects as above. Always remember that these drugs have been known to cause dependency and other adverse effects, especially with long-term use of these drugs. Be careful to monitor the dose of these drugs with long-term use. Also be sure to monitor the effectiveness of the drug with long-term use. Be sure to carefully and slowly withdraw the drug when there has been long-term use.

These drugs are also prescribed and used for other related medical problems. For example, Vistaril can be given alone or is commonly given with Demerol to help enhance effects of analgesia. (As with any drug, if you are unsure of the dosage or use; check with your hospital's pharmacy or the most recent hospital formulary for administering any drug).

This text is a guide and should be used along with your hospital formulary and/or pharmacy. Therefore, be aware of other uses and combinations of these drugs. Watch for any adverse effects. Adverse effects are very common when drugs are mixed, or if patient is already taking other drugs (prescribed or not). Do not use this text as the final guide for the administration of drugs to your patient. The nurse should always use the package insert or the PDR as the final authority for the administration of any drug. These inserts and PDR is the definitive information regarding each drug and its use and adverse reactions.

F Antipsychotic (Neuroleptic) Drugs

We will now present the specific classification of antipsychotic drugs. Previously we presented drugs that are often used in conjunction with antipsychotic drugs.3 It is necessary that each nurse have a good understanding of these drugs before we discuss the antipsychotic drugs, because there is great potential for interaction of these.

The "psychotherapeutic" drugs or "psychotropic" drugs or "neuroleptic" drugs or also called the "major tranquilizers" are used to treat emotional illness characterized by disturbances in thought. This is also the definition of psychosis. The symptoms which must also be treated are: delusions, hallucinations, lack of responsiveness to environment, changes in the mood that are inappropriate to events around the patient, and behavioral aberrations, including performance of strange movements or actions.

As you study this next section, you will find that other related drugs are also included in this section. Other classes of **antipsychotic drugs** are used to treat the neurotic disorders. However, it is very difficult to separate these treatments, as the diagnoses are often not clearly separated. In other words, some patients diagnosed with a neurosis, may also exhibit psychotic symptoms; or Some neuroses are borderline psychotic disorders. Therefore, we will tell you in advance that we are "lumping" many of these drugs into one category so that they are easier to study.

A complete history and physical examination must be completed prior to the administration of these very powerful drugs. A physical assessment is necessary to rule out organic disorders and to define any kidney, liver, and other major diseases.

3 The term "PSYCHOTROPIC DRUGS" is a very broad term that includes all the "MIND" drugs; such as antidepressants, sedatives, hypnotics, and the Antipsychotic drugs The Antipsychotic Drugs, is a very specific group of drugs used to treat Psychosis, a severe mental illness.

General Contraindications and Side Effects of these agents:

Contraindications of the antipsychotic agents include: any history of drug hypersensitivity, severe depression, bone marrow depression or blood dyscrasias, and brain damage. Patients with a history of impaired liver function, cardiovascular disease, hypertension, glaucoma, diabetes, Parkinson's Disease, peptic ulcer disease, epilepsy, or pregnancy should be closely observed when taking these drugs.

General Nursing Implications in Neuroleptic Drug Therapy:

Patients receiving antipsychotic drugs should have an evaluation of blood pressure, complete blood count, liver function tests, and vision tests before therapy and at periodic intervals thereafter.

Be aware of the following precautions:

1. If a single dose is ordered, give oral neuroleptics within one or two hours of bedtime whenever possible to aid sleep. Minor side effects are less bothersome at this time.

2. Avoid contact with concentrated solutions **while preparing them since they** are irritating to the skin and may cause contact dermatitis.

3. Liquid concentrates should be mixed with at least 60ml of fruit juice or water before administration to mask taste of the concentrate.

4. Do not give antipsychotic drugs subcutaneously (SC) unless specifically ordered since they may cause tissue irritation. They should be given as deep intramuscular (IM) injections.

OBSERVE PATIENT FOR:

1. therapeutic effects of the drugs, such as decreased agitation, decreased hallucinations, and increased socialization.

2. a decrease in nausea and vomiting if drug is given as an antiemetic.

3. drug-induced extrapyramidal side effects and early signs of tardive dyskinesia and NMS (neuroleptic malignant syndrome).

4. anticholinergic effects, respiratory depression, hypersensitivity 5. drug interactions

6. signs of agranulocytosis (sore throat, fever, discomfort)

7. drug-induced endocrine-related changes; menstrual irregularities, breast enlargement, lactation, changes in libido.

8. signs of jaundice, high fever, upper abdominal pain, nausea, diarrhea, and skin rash.

Antipsychotic Medications

Class: Phenothiazines: (Aliphatic Derivatives)

1. Chlorpromazine (Thorazine, Promaz, Chloramead, Psychozine)

Actions include:

antipsychotic, acute and chronic antiemetic, sedative, hiccups, for alcohol withdrawal, and many other actions and indications

This drug is the prototype of all phenothiazines in this group. The side effects depend upon the dosage, in low doses, few side effects; in higher doses, extreme side effects and adverse effects can be seen. usual dosage: PO: initial dose 200-1000 mg daily in divided doses; maintenance dosage lower--acute patients, higher dosages. IM dose can be given in acute situation: 25-100 mg IM, extreme hypotension can occur.

2. Promazine HCL, (Norazine, Sparine)

This drug is generally less effective, fewer side effects than Thorazine. It is used as an antiemetic, and for alcohol withdrawal. usual dosage: PO, IM: 50-100mg daily and/or PRN

3. Trifluprom azine, (Vesprin)

This drug is similar to Thorazine, except it is usually less sedating. usual dosage: PO: 50-200 mg. It usually has more side effects. Store in amber colored containers, parenteral solution should be colorless to light amber, do not use darkened solutions.

Piperazine Derivatives

1. Mesiridazine, (Serentil) This drug is usually just as sedating as Thorazine. It has generally fewer side effects, with milder hypotensive effects than Thorazine. Usual dosage is 25-200 mg.

2. Piperacetazine, (Quide)

This drug is usually less sedating than Thorazine. It has fewer hypotensive effects, but will usually have an increase in other side effects, don't use with children under 12 years of age.

3. Thioridazine, (Mellaril)

This drug is the prototype piperidine phenothiazines; sedation and side effects are similar to Thorazine. It has no antiemetic properties; it is a potent anticholinergic; it has the lowest incidence of extra-pyramidal effects; little or no effect on seizure threshold, and can be used for epileptic patients. In large doses this drug inhibits ejaculation. ECG changes can be seen in higher doses, more than with others in classification. Pigmentary retinopathy can occur. Test acuity at intervals. No photosensitivity is seen with this drug, as with others. Jaundice is very rare. It is used with depressed patients, as it will usually not add to depressed states. Usual dosage: PO: 100-300mg daily, higher or lower according to tolerance.

4. Trifluoperazine, (Stelazine)

Do not confuse with trifluopromazine.

This drug has low sedation and low hypotensive effects and low anticholinergic effects. EPS (EPS-Extrapyramidal Symptoms) in high doses especially in patients over 40; low incidence of jaundice and blood dyscrasias; no marked ECG changes as with others of this type; increased pain reported by some angina patients; lower convulsion threshold, caution when patient is epileptic or prone to seizure activity; parenteral solution is colorless to light amber. Usual dosage: PO 5-l0mg IM: 1-2mg q4-6hr, max 10 mg daily in divided doses.

5. Acetophenazine maleate, (Tindal)

This is similar to Stelazine with more sedation effects & fewer side effects, usually. Usual dosage: PO: 20mg TID, up to about 600 mg daily.

6. Carphenazine, (Proketazine)

This drug is similar to Stelazine; more side effects and less hypotensive effects. Dosage: PO: 25-50mg TID max. 400mg daily

*Fluophenazine HCL

is Prolixin, also called Permitil

*Fluphenazine decanoate

is Prolixin Decanoate

*Fluphenazine enanthate

is Prolixin Enanthate

These drugs are similar to Stelazine and Thorazine in action. However, Prolixin is noted for its long-acting duration. Prolixin HCL is shortest acting, rapid onset and action; Decanoate and Enanthate act for about two weeks after oil-based solution is deposited by IM or SC injection. This is especially good for non-compliant patients.

Usual dosage: PO: Prolixin 2.5 - 10 mg daily. IM or SC long-acting: 25 mg q2 weeks, after establishing optimal dosage (dosages will be adjusted according to patient needs and tolerance. First the patient is given larger doses in order to control acute symptoms. Maintenance doses are then determined for each patient).

7. Perphenazine, (Trilafon) This drug similar to Stelazine, less sedating; less hypotensive.

Usual dosage: PO: 16-64mg daily in 2-4 doses IM: 5-l0mg Q6h max 15mg/24 hours. Oral liquid form should be mixed with suitable juice for administration; parenteral solution, protect from light--color should be clear or light amber.

8. Prochlorperazine, (Compazine)

This drug is more often used as an antiemetic. It can be used for sedation. It is for oral and parenteral use. Elderly and debilitated are more susceptible to this drug. The sc injection gives local irritation, not recommended for sc. Some discoloration of the solution is acceptable. Do not use if markedly discolored with oral forms of solution.

Usual dosage is: oral tablets 5-15 mg, act in about 30-40 minutes, 3-4 hours duration, time release, oral 5-15 mg act in 30-40 minutes, 10-12 hours duration, IM injection 10-20 mg, act in 10-20 minutes, 3-4 hours duration. Rectal suppository 25-50 mg, act in 60 minutes, 3-4 hours duration.

Thioxanthene Derivatives:

1. Chlorprothixene, (Taractan)

This drug is similar to chlorpromazine, has a heavy sedative quality and thixene and aliphatic derivatives hypotensive effects; fewer extra pyramidal effects; appears to be more effective for the treatment of acute rather than chronic schizophrenia; not proved safe in pregnancy or use in children. Dosage: PO: IM: 25-50mg 3-4 times; maximum of 600 mg daily.

2. Thiothixene, (Navane)

This drug is similar to trifluoperazine and other piperazines. It is usually less sedating; usually less hypotensive effects; but just as much potential for adverse effects. Usual dosage: PO: 2-5 mg 3-4 times daily; IM: 4 mg 2-4 times daily.

Butyrophenone Derivatives:

1. Haloperidol, (Haldol)

This drug indicated for acute & chronic psychoses, mania, **tics & vocal** utterances of Gilles de la Tourette syndrome; severe behavioral disorders of children hyperexcitability. Is similar to piperazine group; lower sedation; less chance of adverse effects than most; less chance of anticholinergic effects higher incidence of EPS; minimum long-term effects, does lower seizure threshold. Usual dosage: P0: 0.5 - 5 mg 2-3 times daily, IM: 2-5 mg.

Other (Miscellaneous) Drugs:

- **Molendone HCL,** (Moban, Lidone); This drug is a dihydroindolone that blocks postsynaptic dopamine receptors in the brain. 50mg up to a maximum dose of 400mg per day, P.O. (Usual interactions and side effects of other psychotropics)

- **Droperidol,** (Inapsine, Droleptan) usually given as a 5mg IM dose for the management of severe agitation of psychotic disorders. Side effects may include: hypotension, tachycardia, extrapyramidal reactions

- **Loxapine,** (Loxitane, loxapac); indicated for psychotic disorders; dosage: 60mg to 100mg daily, P.O.

- **Pimozide,** (Orap); This drug works by blocking dopamine receptors. Maintenance Dosage: 7mg to 16mg per day. Antipsychotic effects take two weeks or longer to achieve.

G Atypical Antipsychotic Medications

- **Clozapine,** (Clozaril); This drug is indicated for schizophrenia in severely ill patients who were unresponsive to other therapies. Dosage starts at 25mg and may increase up to 300mg or 40omg per day in some cases.

- **Olanzapine,** (Zyprexa) is a new medication used to treat schizophrenia. In general this drug has fewer side effects than many of the others in this classification. Side effects include: dizziness, drowsiness, weight gain, constipation, headache, akasthisia, tremors.

***New Chemical Classifications**:

Benzisoxazole Derivatives: (antipsychotic drug classification)

• **RISPERDAL (risperidone)** Janssen Pharmaceuticals; The exact mechanism of this drug is not known. However, it is proposed that this drug action is mediated through a combination of dopamine type two (D2) and serotonin type two (5HT2) antagonism.

Risperdal is indicated for the management of the manifestations of psychotic disorders. Dosage: lmg to 6mg per day in divided doses (see below)

Precautions of this drug include:

1. NMS, Neuroleptic Malignant Syndrome--a potentially fatal symptom complex which has been reported with this and other antipsychotic drugs; symptoms include; hyperpyrexia, muscle rigidity, altered mental status, and autonomic instability (irregular pulse, irregular blood pressure, tachycardia, diaphoresis, arrhythmias)

2. Tardive Dyskinesia
3. Proarrhythmic Effects--QT interval lengthened
4. orthostatic hypotension
5. seizures
6. hyperprolactinemia
7. cognitive and motor impairment

Dosage: Usual initial dose:

day 1	1.0 mg BID
day 2	increase to 2.0 mg BID
day 3	increase to 3.0 mg BID

*up to 16 mg per day may be used in some cases under careful supervision

Choosing the Correct Antipsychotic:

The reason we included this section, is to tell you that there is no one guide to selecting the best drug in these categories. The list above is by no means a complete list of psychotropic drugs, there are many others to choose from. However, most of the antipsychotic drugs are surprisingly equal to Thorazine. Each drug derivative has its own particular chemical activities. One physician will prefer one drug over another.

Several factors will help the MD make a decision on which drug(s) to use:

General findings:

1. patient's symptoms and diagnosis 2. patient's physical exam & history

Specific findings:

1. the patient's reaction to specific drugs (trial and error) 2. patient compliance
3. idiosyncracies

Once all factors have been considered, the MD will choose the best possible drug therapy and dosage of the drug (s). Another great consideration, as mentioned earlier, is the side effects, adverse effects, and EPS that each drug may cause. The MD will have to examine all adverse reactions to drugs, especially those reactions that can be dangerous.

Nursing Considerations:

1. Prior to initiating therapy, and again at periodic intervals thereafter, a general examination should include evaluation of blood pressure, liver function and the eyes, and a complete blood count.

2. Postural hypotension, dizziness, sedation are common during the first few weeks of chlorpromazine therapy. Changes in position should be made slowly, especially from the recumbent to the upright position; the patient should dangle legs prior to ambulating. IM preparations should be slowly injected; patient should remain in recumbent position for at least one hour.after parenteral medication.

3. Avoid contact with skin, eyes, clothing. Contact dermatitis was reported.

4. Observe the patient for EPS such as mentioned in the text; you can even expect other unusual related symptoms, as each person reacts differently.

5. Observe and report early signs of tardive dyskinesia, including involuntary movements of mouth, lips or tongue.

6. Observe menstrual irregularities, breast engorgement, lactation, changes in libido (increased in women, decreased in men). Reassure patient that such effects are induced by the drugs and are usually temporary.

7. Observe and report early symptoms of cholestatic jaundice; a high ever, upper abdominal pain, nausea, rash, diarrhea. Withhold drug and report if these signs appear: yellowing of skin, mucous membranes, or sclera.

8. Alert patient about side effects that should be reported; fever with sore throat, and weakness (suggests blood dyscrasias), change in vision, change in tolerance to heat or cold.

9. Abnormal pigmentation of skin induced by chlorpromazine in presence of sunlight may be prevented by wearing protective clothing over exposed areas.

10. Many weeks may be required before the beneficial effects of some drugs may be clearly manifested. Teaching patient and/or family the importance of continuing to take the prescribed medication as directed and remain under close medical supervision is essential for treatment success.

11. After chronic therapy, drug should be slowly withdrawn over a period of several weeks to minimize risk of an exacerbation of the psychotic state or appearance of tardive dyskinesia.

H Side Effect Medications

Summary of the psychotropic Medications & Side Effects:

The term "antipsychotic drug" refers to those classes of drugs specifically used to combat psychosis. The major clinical use of antipsychotic agents or Neuroleptic drugs is in the treatment of psychoses such as schizophrenia, mania, paranoid disorders, organic dementia, and acute brain syndromes. Symptoms include impaired communication or the inability to relate to others, delusions, hallucinations, lack of responsiveness to the external environment, and the inability to identify reality.

Antipsychotic agents provide symptomatic control of the patient by blocking the activity of dopamine, a chemical normally occurring in the brain and having the potential to produce psychotic thinking. Too much dopamine causes nerve impulses in the brain stem to be transmitted faster than normal, resulting in strange thoughts, hallucinations, and bizarre behavior. Blocking this activity of dopamine lessens or prohibits the development of such thoughts and behavior. In addition to this property, antipsychotic agents have antiemetic properties; they have been used to treat intractable hiccoughs, and have been used in combination with other drugs for pain control. The antipsychotic drugs were first introduced in 1951 with the development of Thorazine, the prototype drug. Additional phenothiazine and non-phenothiazine antipsychotics have been developed and are in use today.

Contraindications and Side Effects:

Contraindications of the antipsychotic agents include: any history of drug hypersensitivity, severe depression, bone marrow depression or blood dyscrasias, and brain damage. Patients with a history of impaired liver function, cardiovascular disease, hypertension, glaucoma, diabetes, Parkinson's Disease, peptic ulcer disease, epilepsy, or pregnancy should be closely observed when taking these drugs.

General side effects include:

1. drowsiness, lethargy, inactivity; avoid driving, avoid operating dangerous machinery

2. dry mouth, nasal congestion, blurred vision

3. skin reactions like urticaria or dermatitis

4. pigmentation of the skin and eyes, photosensitivity or phototoxicity

5. constipation or urinary retention

6. general orthostatic hypotension during the first two weeks of treatment

7. alteration in sexual functioning owing to a diminished sex drive

8. seizures due to a lowered seizure threshold

9. agranulocytosis (usually during the first eight weeks of treatment)

10. hyperglycemia

11. mild ECG changes

12. gastrointestinal distress such as nausea or heartburn

13. weight gain

14. edema

Although this list of side effects is lengthy, they are generally mild effects. These side effects can, however, be annoying to the patient. They should be treated as soon as they are recognized to prevent them becoming severe.

Extrapyramidal Side Effects:

Extrapyramidal side effects (EPS), or adverse neurological effects may occur during the early phase of drug therapy. These symptoms are classified as parkinsonism (not true Parkinson's Disease), akasthisia, and acute dystonic reactions. Tardive dyskinesia may occur following short-term use of moderate doses, although it generally occurs after long-term use and highdose therapy. Some patients may have other unusual EPS and acute reactions to these drugs. These include muscle stiffness and "posturing" or inability to move as well as other symptoms. Be alert to changes in patient condition.

Parkinsonism (not true Parkinson's Disease)

This side effect involves motor retardation or akinesia, Masklike facies, rigidity, tremors, "Pill-rolling," or salivation. These symptoms generally occur after 1st week of treatment or before the 2nd month. Treatment for these effects usually includes administration of anticholinergic drug therapy.

Akathisia (motor restlessness)

This is a constant state of movement characterized by restlessness, difficulty sitting still, or strong urge to move about; sometimes referred to as "walkies and talkies." This generally occurs two weeks after treatment begins. Rule out anxiety before administering anticholinergic therapy.

Acute Dystonic Reactions

This is characterized by irregular, involuntary spastic muscle movement, wryneck or torticollis, facial grimacing, abnormal eye movements, or oculogyric crisis (backward rolling of eyes in the sockets). This may occur at anytime from a few minutes to several hours after the first dose of antipsychotic agents. The treatment would be to administer an anticholinergic agent. Have respiratory support equipment readily available if needed.

Tardive Dyskinesia

This is probably the most frequently seen serious side effect occurring during abrupt termination of the drug or after reduction in dosage after long-term, high-dose therapy. It is characterized by involuntary, rhythmic, stereotyped movements, protrusion of tongue, puffing of cheeks, chewing movements, or involuntary movements of the extremities or the trunk. There is no specific treatment except to discontinue use of antipsychotic drugs. This occurs in about 3% of patients who take antipsychotic drugs. If not detected early, symptoms may persist for years or the syndrome may be irreversible.

Neuroleptic Malignant Syndrome (NMS)

This is a rare syndrome that is a potentially fatal complication of neuroleptic treatment. It is considered to be an idiosyncratic reaction rather than a toxic reaction. It has been reported in patients never exposed to neuroleptics. NMS may develop within hours or after years of continued drug exposure. Symptoms include hyperpyrexia, severe muscle rigidity, altered consciousness, alterations in blood pressure, tachycardia, difficulty swallowing, or elevated white blood cell count. The treatment is symptomatic. The symptoms exhibited by the patient are treated and then the neuroleptic drug is gradually reduced. However, some authorities suggest to immediately stop the drug and restart at the lowest possible dosage.

Drucrs used to treat Extrapyramidal symptoms (EPS)

The exact mechanism of action of these drugs below is still unclear, but they are thought to act by blocking dopamine at the receptor sites in the limbic system as well as in the hypothalamus and extrapyramidal system tracts. As result, CNS arousal responses are diminished and excessive perceptual input is decreased. The impact of this group of drugs on the reduction and control of symptoms of schizophrenia and other thought disorders is well known. Agitation, rage, and sexual impulses are suppressed promptly after therapy is initiated, and with the suppression of hallucinations, delusions, and paranoia can occur within 2 to 21 days.

Individualization of dosage is dependent on observation of the clients response to medication and the side effects experienced. The risk of irreversible extrapyramidal effects (tardive dyskinesia) mandates identification of the lowest medication dosage which provides optimal symptom relief. These drugs are used to treat the Parkinson-like symptoms (EPS) that the patient can suffer from the long-term use of the antipsychotic drugs.

Some symptoms seen in this disorder are:

fatigue, drowsiness, drooling, shuffling gait, tremors, and other symptoms seen in true Parkinson's Disease.

- **Trihexyphenidyl HCL,** (Artane), thought to block central cholinergic receptors, helping to balance cholinergic activity in the basal ganglia. Dosage: 6mg to l0mg P.O. daily.
- **Diphenhydramine,** (Benadryl), This common antihistamine is also used for treating EPS/acute dystonic reactions. Dose: 25mg to 100mg P.O. daily.
- Benzotropin, (Cogentin, Bensylate, APO-Benztropine), this drug blocks central cholinergic receptors, helping to balance cholinergic activity in the basal ganglia. Acute Dystonic Reaction Dosage: 1mg to 2mg BID daily. (Acute Dystonic Reaction and EPS are often used interchangeably)
- **Propranolol,** (Inderal), is a beta-adrenergic blocker drug used to treat hypertension and angina pectoris. This drug is also used to treat migraines and Parkinson's symptoms as well. This drug has many cardiovascular side effects so monitor patients carefully.
- Amantadine, (Symmetrel), is an antiviral drug that is also used to treat Parkinson's symptoms. Dose: 100mg to 300mg P.O. daily in divided doses.

CHAPTER III

Issues in Pharmacology and Select Disease Conditions

DRUG ABUSE UPDATE

The problem of drug abuse has been with us for quite some time. Recently, there have been a number of programs developed for treating addictions to alcohol, drugs, tobacco and others. Many of the new programs center around the way people adjust to their addictions, and finding a new and positive addiction to replace the bad ones. There are physiological and psychological aspects to all addictions. It is also recognized that more and more professionals must be treated for addictions. Programs are in our schools now, and professional organizations and businesses are forming programs to deal with the problem.

Talwin Nx, Pentazocine, is a new formula developed by the company to try to stop the abuse of Talwin 50mg tablets formerly used. To **abuse the drug,** many persons would grind the tablet and mix it with other common drugs in order to obtain the additive effect of the drugs, when injected, and become "high." Now the company has mixed Narcan, a narcotic antagonist, in with the drug. When taken by mouth, the normal method, as prescribed, the Narcan in the drug is inactivated by the stomach acid. The patient gets the full benefit of the drug as they were supposed to. However, if the person tries to abuse the drug by injecting it, the Narcan in the mixture stops the drug from giving them their "high."

The only potential problem with the new drug, is that of withdrawal symptoms. If the regular heroin or narcotic user injects this drug, the Narcan can block the effects of the drug the person takes. They could develop severe withdrawal symptoms requiring treatment. Be aware of the possible withdrawal symptoms.

Naltrexone Hcl. Trexan, is the first oral narcotic antagonist approved to treat narcotic addiction. This drug is administered to the person after total detoxification from the narcotic. It is reported to reduce the cravings for narcotics and to help reduce the cases of re-addiction to narcotics. The drug has shown to be most effective in those motivated to stop the addiction. Combinations of Trexan and other therapies are ideal (group therapy, individual therapy etc.).

Nurses and doctors are also at high risk for drug addiction. The reasons are multiple. Easy access to drugs and high job pressures are just two of the many reasons for addiction to drugs and/or alcohol by health professionals. If you recognize the problem, talk to the person and refer them to a professional who can help. If the co-worker is affected by the addiction, you may have no choice but report the problem. If the addiction has not yet affected their work performance, you should first talk to them and let them seek help on their own. The "pressure" you put on them depends upon how well you know the person. You would certainly very "strongly" urge your own family member to get help. However, with a co-worker you must be careful that the "pressure" cannot be construed as legally slanderous or otherwise improper. Consult a professional in this area if you are unsure as to what to do. However, do not ignore the problem.

Select Topics in Pharmacology:

Legal Issues:

Recent surveys show that the most common reason for litigations brought against nurses is pharmacology related. Most patients and/or families will sue due to death or injury from drug side effects, insufficient treatment, and insufficient or infrequent reassessment of the prescribed drug therapy. Since you are participating in this course, you are involved with a continuing education activity that will help you to prevent certain medication-related errors.

Timolol Eye Drops---

Timolol eye drops are used to **reduce intraocular pressure** in cases of glaucoma and certain other related conditions. It is classified as a topical beta-blocker and is used mostly to treat glaucoma. Recently it has been reported to have caused **sexual dysfunction in men and women.** The usual side effects of the drug are **dyspepsia, hypotension, fatigue, confusion and headache.** These side effects are due to the fact that the drops can be **absorbed systemically.** Other symptoms include impotence, decreased libido, and also decreased ejaculation volume. The symptoms usually disappear when the drug is discontinued. Patients should be informed of these possible systemic effects.

A recent article has shown that a very high percentage of errors have been made when administering this drug into the eyes. Several nurses inadvertently picked up and administered Hemoccult developer solution instead of Timoptic eye drops. Of course, this is considered to be a gross medication error. This type of error could easily be prevented by simply reading the label carefully. However, nurses should be careful when the patient is being tested for occult blood in the stool and who are also being administered eye drops. Do not leave these two bottles near the bedside where it could be picked up accidentally.

9

Oral Contraceptives **An Overview:**

These following oral hormones are probably the most common types of artificial birth control in the country.

The two main types are:

(a) combination pill, containing estrogen and progestin; taken for the entire 21 days of the menstrual cycle

(b) "mini-pill" contains only progestin, it must be taken every day.

They produce contraception by inhibiting ovulation. FSH (follicle stimulating hormone), a pituitary hormone, is blocked and subsequently no follicle develops. The release of the FSH is blocked by the pills containing estrogens. Progestins inhibit the pituitary release of LH (luteinizing hormone).

This is the hormone responsible for release of the ovum from the follicle. The hormones then, either singly or together, interfere with the ovulation process. There are additional contributory factors to inducing contraception. The estrogens and Progestins also alter cervical mucus. It becomes thicker and adversely affects the sperm migration.

Sperm mobility is also affected by the changes in **the uterine and oviduct mus-**cles; the ovum and sperm transportation is adversely affected. The endometrium is altered adversely to the implantation of the fertilized ovum.

Almost half of the users of the oral contraceptives will suffer some type of side effects. The most common side effects are headaches, nausea, weight gain, spotting, mood alterations, depression, fatigue, chloasma and others. There are other adverse effects and other contraindications listed below.

Side effects

Side effects can best be classified according to the time of onset and duration. Note especially, the effects even after discontinuation of the drug.

We have added a classification according to severity of symptoms:

class (1)
minor s/e and symptom usually is temporary

class (2)
minor s/e and symptom usually will last a long time

class (3)
major s/e and symptom usually is temporary

class (4)
major s/e and symptom usually will last a long time

class (5)
*may cause permanent damage

First 2 to 3 months:

class (1)

nausea, dizziness, mild edema

class (2)

weight gain, breast fullness & tenderness

class (3)

thrombophlebitis (legs), breakthrough bleeding

class (4)

elevated serum lipids

class (5)

thrombophlebitis (pulmonary emboli, pelvic vein and/or the retinal vein)

After the first 3 months:
(longer time periods)

class (1)

headaches, anxiety, fatigue, elevated thyroid function studies

class (2)
depression, increased fatigue, blurred vision class (3) increased weight gain, vaginitis, myomas, decreased menstrual flow class (4) hirsutism, spider angiomata, pelvic relaxation, cystocele, rectocele class (5) arterial thrombosis--visual disturbances; possible stroke, chloasma

After Discontinuation, the following may occur as complications to long-term use of the oral contraceptives:

infertility, amenorrhea, hypothalamic and endometrial suppression, a type of acne, and alopecia, and others

There are many other side effects experienced by many women taking these pills. They are very many and varied, especially related to the hormone changes. Hypertension is common; breast changes are common; oily skin, cramps, itching and many others.

The most common oral contraceptives:

Combination Types: (Progestins & Estrogen combinations)
1. Brevicon (ethinyl estradiol and norethindrone)
2. Norinyl (ethinyl estradiol and norethindrone)
3. Demulen (ethinyl estradiol and ethynodiol diacetate)

4. Ortho-Novum (ethinyl estradiol and norethindrone)

5. Desogen (ethinyl estradiol and desogesterel)

6. Ovcon (ethinyl estradiol and norethindrone)

7. Loestrin (ethinyl estradiol and norethindrone acetate)

8. Norlestrin (ethinyl estradiol and norethindrone acetate)

9. Levlen (ethinyl estradiol and levonorgestrel)

Progestin Only Types:

1. Ovrette 2. Micronor 3. Nor-QD

ADMINISTRATION: The nurse should remember that these pills actually contain many different hormones. There are several different estrogens and several different progestin compounds which might be in the particular brand of pill. Avery detailed patient history is imperative before the MD will prescribe a particular kind of pill. The nurse must always be alert to the patient historical information; to help make the decision for which brand is best for the patient.

Most combination contraceptives will begin on the first Sunday after the menses. Take one pill daily, at the same time each day. If 21-day packs are used, wait a week to start the next pack. If 28-day packs are used, no wait is necessary. The woman should be advised to still use another form of contraception during the first month, because protection will not be built up enough. Minipills are started on the first day of menstruation. Then take one pill daily, every day, at the same time every day. Missed pills should be taken as soon as possible. If you miss more than one pill, make up the difference as instructed. If any of the pills are missed, you should use an additional form of contraception until your next pack begins, or next period. Always consult MD for missed pills, and instruct the patient to report any adverse symptoms.

Other Considerations:

A complete physical exam and gynecological workup are performed before prescribing the drugs. Pills should be discontinued two weeks before elective surgery in order to decrease the incidence of thrombosis post-surgery. Serum cholesterol may be elevated or decreased in some women. Glucose intolerances have been noted in some. Increases in circulating thyroxine, proteins, PBI and T_4 have been noted. Many other hematology results can be affected, including coagulation studies and blood plasma components. The drugs may interact with other drugs, always check if patient is taking other meds.

Contraceptive Implant:

Norplant has been approved by the Food and Drug Administration. The contraceptive inhibits ovulation and thickens the cervical mucus. Six thin cylinders of the progestin levonorgestrel are inserted beneath the skin of the upper arm. They are removed after five years and, if needed, replaced. The cumulative pregnancy rate over five years is 1.1°i.

More studies are being done on these implants due to an increase in reported side effects and pregnancy. It has been reported that there are many side effects such as bleeding, headaches, nausea, and other side effects attributed to the drug. Some studies have shown that Norplant works well and prevents pregnancy. Other studies have discovered a variety of side effects and local effects from the drugs. We will report on these studies when they are completed. As with all contraceptives, the nurse should instruct the patient to consult their MD before deciding on which method to use.'

Emergency contraception (Morris 2000)

In 1998, the FDA approved Preven, the first dedicated emergency contraception product. Preven is a combination of 0.05 mg ethynyl estradiol and 0.25 mg levonorgestrel. There are two pills per dose. The first dose is taken within 72 hours of unprotected intercourse and the next dose is taken in twelve hours.

In July 1999, the FDA approved "Plan B,11 the first dedicated progestin-only pill developed in the U.S. to prevent pregnancy after unprotected intercourse .s Plan B, which is for women who don't want to take estrogen, consists of two 0.75 mg tablets of levonorgestrel to be taken 12 hours apart, the first one within 72 hours of unprotected intercourse. Plan B has been shown to be more effective than the previous estrogen-type pills and has been shown produce fewer side effects. The only non-hormonal method of emergency contraception is the insertion of a copper T380A IUD within five days of unprotected intercourse.

Side effects most often seen with Plan B are nausea and vomiting. These can be minimized by taking the pills with food or by taking an antiemetic one hour before the first dose. Patients should be warned that after taking hormonal contraceptives, their next period may be earlier or later than usual, and their flow may be lighter or heavier. Irregular menstrual bleeding may occur after the emergency contraceptive dose. Patients who have NOT started menses two or three weeks after the use of emergency contraception should return to their provider for a pregnancy test.

Other side effects include breast tenderness, headache, abdominal pain or cramps, or dizziness. Emergency contraception therapy is safe and can be rQpeated when needed, but patients should be advised not to rely on it as a regular method of contraception; because it is less effective for preventing pregnancy than are other birth control methods.

Recently, there has also been a "movement" to have these pills available without prescription. Each nurse should be aware of any pending legislation to make this happen. Nurses may be called upon to give advice on emergency contraception and should keep informed. We will also report any further information in our course updates in the future.

[4] Remember that there is still great controversy over the use of ANY contraception. Taylor College or this author **do not intend to recommend or not recommend contraception or any particular type of contraception.** Be sure your patient has access to religious/spiritual counseling, as well as the medical aspects of contraception.

[5] Prior to 1999, there were emergency contraceptives available. However, "PLAN B" was the first approved in the U.S. using progestin formulas only.

Hepatitis Update

Hepatitis B immune globulin (human) is still being used to provide the immediate passive immunity for those exposed to risk of hepatitis B. It is administered IM, at 0.06 ml/kg for most adults. That dose would be about 35ml for most people. It should be administered to the person as soon after the initial exposure as possible. Most authorities agree it should be administered within seven days of exposure and repeated 28 to 30 days after the exposure.

Hepatitis B Vaccine:

A breakthrough in recent years, has developed a vaccine to introduce an active immunity to those individuals at risk of exposure to Hepatitis B. Heptavax-B can be administered to adults and children over three months of age with relative safety, according to manufacturer. Persons at risk include dentists, oral surgeons, dental hygienists, and medical personnel (have frequent exposure to blood or blood products), hemodialysis patients, homosexually active males, and several others. The administration of the vaccine has doubtful effect if the exposure has already occurred.

The vaccine is usually given in two or three injections of 1 to 2 ml initially. Boosters may be necessary for children at 5:00 year intervals. It has recently been shown that the injections should be given in the deltoid instead of in the buttocks. (Recommended by the Immunization Practices Advisory Committee of the U.S. Public Health Service). Health care facilities in many states now require employees to take the immunization or show cause why they do not need it (had hepatitis, etc.).

The immunization apparently has a higher rate of effectiveness if given in the deltoid for some unknown reason. It is thought that the injections in the gluteal region do not reach the muscle all the time. Many injections have been shown to be deposited into the fat in the gluteal region instead of the muscle. Absorption of the vaccine from the fatty tissues is very poor, hence, poor results from the vaccination.

Mild side effects have been reported of pain and swelling at the site, along with tenderness and redness. Other side effects might include fatigue, malaise, nausea, dizziness, headaches, myalgias, and skin rashes. At this time, pregnancy is not a contraindication for administration, according to manufacturer. Of major concern today is the AIDS virus. There is no evidence that the virus is transmitted via the vaccine. The process used to manufacture the vaccine has been shown to destroy the AIDS virus and all related viruses.

Most recently, the CDC has recommended that the Hepatitis vaccine now be given routinely to all newborn infants. This is a tremendous step in helping to control the epidemic of Hepatitis B. We will present more information as it becomes available. However, many hospitals have begun to routinely immunize newborns at birth.

Drugs Used to Treat HIV/AIDS:

There are five main drugs now used for fighting the HIV virus itself. These drugs are AZT, ddI, ddC, 3TC and d4T. These drugs are used alone or in combination to slow or temporarily stop the reproduction of the HIV virus. These "antiretroviral" drugs are very similar in action. They all have been shown to increase CD4 cell counts or slow their decline, increase body weight, improve other laboratory indicators of HIV disease, and delay or reduce mental or neurological impairments. They don't work for everyone and they don't work in the same way for everyone.

Please note: There are several new drugs now approved to fight the HIV virus. These will be mentioned in this chapter. However, these are still the four main drugs used today. The new protease-inhibitors and other drugs are rapidly becoming more used and may soon overtake the use of some of these drugs. We will update this as new information is available.

Summary; Drugs used to treat the HIV Virus:

Usually, AZT is the first drug used to treat the HIV viral infection. Remember that the opportunistic infections are totally separate from the HIV virus. Opportunistic infections must be treated as they appear.

If AZT fails to control the virus, then one of the other drugs will be given. The patient will have periodic blood tests to see if the drug is working. If the CD4 cell counts continue to drop, or severe side effects are seen, AZT is stopped and another drug (or combination) will be tried.

If AZT fails, the MD will then usually try ddI alone or the combination of AZT and ddI. If this combination fails to work, then the MD will usually try AZT and ddC. Remember, that ddC must be used in combination with AZT at this time. ddI combined with AZT also appears to be better than AZT alone according to several recent studies.

Next, d4T will be used alone, after AZT fails (or patient is intolerant to AZT). Next, the AZT and d4T combination could be used. Remember that d4T also cannot be used with ddI or with ddC. However, d4T does offer another alternative to AZT alone or to the other combinations of drugs.

Other Drugs and Drug Combinations:

Combining AZT with the anti-herpes drug acyclovir raised CD4 counts higher and longer that AZT alone in a U.S. study and provided a survival benefit after one year in an international study. AZT combined with injections of alpha-interferon may be better that AZT alone, based on four other studies. ddI, ddC, and d4T produce peripheral neuropathy, the three drugs should not be used in any combination.

A three-drug combination that included the Hoffmann-La Roche protease inhibitor, saquinavir, used in combination with AZT and ddC yielded better results that the drug combined with only AZT. It also worked better than AZT combined with ddC. Saquinavir--a protease inhibitor--raised CD4 cell counts and lowered virus in the blood, according to a study of 302 patients sponsored by the U.S. National Institute of Allergy and Infectious Diseases.

These combinations and other drug combinations will be studied further. There are many studies going on right now that will test various drug combinations. We will report these findings as they become available.

NOTE: Protease Inhibitors:

(Phillips 1996) In 1995, a new classification of drugs, the protease inhibitors, was added to the armamentarium for treating HIV infection. Although the data are limited, early evidence suggests that a combination of reverse transcriptase inhibitors and protease inhibitors delays the progression of HIV disease and prolongs the lives of HIV-infected people.

Proteases are enzymes that split the peptide bonds of larger proteins into smaller proteins. HIV protease helps HIV mature. HIV protease autocleaves itself from the precursor protein gp160. Following autocleavage, gp160 is cleaved into the two glycoproteins of the viral coat. Then, HIV protease promotes maturation of HIV by splitting retroviral precursor polyproteins into structurally essential glycoproteins and proteins. Thus, HIV protease allows immature, noninfectious virions to become mature, infectious virions.

Protease inhibitors prevent maturation of newly formed virions by preventing the cleavage of HIV's polyproteins. Thus, protease inhibitors prevent immature, noninfectious viruses from becoming mature, infectious ones. Many antiretrovirally active protease inhibitors have been developed. The three protease inhibitors (saquinavir, ritonavir, indinavir) that have been approved by the FDA will be presented here.

Saquinavir:

Saquinavir mesylate is indicated for the treatment of advanced HIV infection in combination with other nucleoside analogues such a zidovudine (ZDV) and zalcitabine (ddC). Clinical trails data that defined the indication and use of saquinavir were only based on the combination therapy of saquinavir with either ZDV or ddC.

The recommended dosage of saquinavir is three 200 mg capsules taken three times a day (600 mg TID) in combination with a nucleoside analogue. The recommended dosages of nucleoside analogues are: zidovudine 200 mg three times a day orally or zalcitabine 0.75 mg three times a day orally. Saquinavir in dosages of less than 600 mg three times a day is not recommended. Saquinavir therapy should be interrupted for toxicities known to be associated with saquinavir therapy. Dose adjustment of the nucleoside analogues should be based on the toxicity profile of the individual nucleoside analogue that is causing the toxicity.

The most frequently reported adverse reactions in patients receiving saquinavir were diarrhea, abdominal discomfort, and nausea. Rare instances of some adverse reactions have been reported: confusion, ataxia/weakness, acute myeloblastic leukemia, hemolytic anemia, attempted suicide, Stevens-Johnson syndrome, seizures, serious cutaneous reactions, elevated liver enzymes, and exacerbation of chronic liver disease.

Saquinavir has been associated with significant increases in CD4+ cell counts and few side effects. It is usually used in combination with either AZT or a nucleoside analog. Saquinavir is more effective in combination with AZT when the client has not taken AZT previously. Since AZT has been widely prescribed in the HIV-infected cohort, some clinicians believe it may be most beneficial to combine saquinavir with either zalcitabine (ddC) or didanosine (ddI).

Saquinavir should not be administered concomitantly with rifampin. Concomitant administration of phenobarbital, phenytoin, dexamethasone, and carbamazepine with saquinavir also may reduce plasma levels of saquinavir. If therapy with these drugs is necessary, alternative medications of the same drug classification should be used if the patient is receiving saquinavir. Patients receiving saquinavir with calcium channel blockers, clindamycin, dapsone, quinidine, or triazolam should be monitored for toxicities of these drugs. Antihistamine therapy should not include terfenadine or astemizole.

Ritonavir has been associated with significantly increased CD4+ counts, increased CD8+ counts, increased responsiveness to new antigens as measured by phytohemagglutinin antigen (PHA) mitogen blastogenesis, increased responsiveness to previously encountered antigens, and decreased viral load. Following treatment with ritonavir, significant decreases in CD4+ cells bearing a CD38 receptor site following treatment with ritonavir have been observed; this may be a very important finding, since an increase in these cells is associated with disease progression.

Indinavir, in clinical trials, dramatic reductions in viral load and improvements in CD4+ cell counts have been reported in clients receiving indinavir. In fact, used in combination with AZT and 3TC, viral loads can be reduced to undetectable levels.

Protease inhibitors have shown effectiveness when used as a monotherapy. However, synergistic effects have been demonstrated when reverse transcriptase inhibitors and the protease inhibitors are combined. The term synergy identifies the concept that the beneficial effects of two or more drugs are greater when the drugs are combined than would be expected if either of the drugs was used alone. Synergistic effects have been noted when certain reverse transcriptase inhibitors are combined: (1) zidovudine, AZT and lamivudine, (lamivudine, formerly known as 3TC) (2) zidovudine, AZT and didanosine, dbl and (3) zidovudine, AZT and zalcitabine ddC. HIV's ability to develop resistance to drugs is a major obstacle to effective treatment. The term resistance refers to the concept that a previously effective antiretroviral drug becomes ineffective due to viral mutations. Viral mutations and subsequent resistance may be slowed by using a combination of drugs. For instance, resistance of HIV to AZT may be delayed by combining AZT with a protease inhibitor or lamivudine. In cross-resistance, development of resistance to one drug results in the development of resistance to other drugs of the same classification or other classifications. Cross-resistance is extremely problematic in HIV infection. Resistance to one protease inhibitor may result in cross-resistance to other antiretroviral drugs, in particular other protease inhibitors. A mutation of only one genetic sequence results in cross-resistance to stavudine, didanosine, and dideoxycytidine. The term resistance-reversal connotes the concept that the development of resistance to one antiretroviral drug undoes the resistance that has developed to another drug. An example of this is the phenotypic resistance-reversal noted in the coadministration of zidovudine and lamivudine.

Saquinavir, plus zidovudine, plus dideoxycytidine.

Phase II clinical trials indicate that combinations of saquinavir (SQV), zidovudine (ZDV), and dideoxycytidine (ddC), synergistically decrease HIV replication. In a study conducted by Collier et al., three treatment regimens were used: (1) SQV, ZDV, & ddC (2) ZDV, & ddC and (3) ZDV, & SQV. Patients receiving a combinations of SQV, ZDV, and ddC demonstrated the greatest increase in CD4 cell counts and the greatest decrease in viral load.

Ritonavir, plus zidovudine, plus zalcitabine.

The effects of a six-month regimen of ritonavir, plus zidovudine, plus zalcitabine were studied in a group of 21 patients. Viral load decreased to undetectable levels in 5 of the 21 participants.

Indinavir, plus zidovudine, plus lamivudine.

HIV viral load decreased to undetectable levels over a four month treatment period in 20 of 22 clients taking zidovudine (AZT), plus lamivudine (3TC), plus indinavir. The participants in this study had an average CD4 cell count of 175/mm3. In a separate study, a six-month course of indinavir, zidovudine, and lamivudine lowered HIV viral load to undetectable levels in 11 of 19 patients. The participants were previously untreated and had an average CD4 lymphocyte count of 150.

Summary:

No major toxicities have been observed as a result of taking either of the three approved protease inhibitors. However, coadministration of ritonavir and nonsedating antihistamines, sedative hypnotics, or anti arrhythmics may produce lifethreatening situations such as oversedation, respiratory arrest, or cardiac arrest. Coadministration of these drugs with protease inhibitors other that ritonavir has led to similar life-threatening reactions. Always identify all the drugs the client is taking before prescribing or administering ritonavir.

Norvir: (Abbott Laboratories, 1997)

The FDA has just approved Norvir, a protease inhibitor, for use in children with HIV and AIDS. Norvir is one of the first of*currently marketed protease inhibitors to receive FDA clearance for use in children with HIV and AIDS. The drug is-one of the first-generation protease inhibitors that has been shown to have a positive impact in the lives of AIDS patients.

The recommended dosage of Norvir in children, in combination with nucleoside analogues, is 400 mg/m2, twice daily, and should not exceed 600 mg, twice daily. The starting dose is 250 Mg/M2, twice daily, which should be titrated to 400 mg/m2. The evaluation of the antiviral effect of Norvir in children is ongoing.

Norvir is currently indicated in adults in combination with nucleoside analogues or as monotherapy for the treatment of HIV infection when therapy is warranted. For patients with advanced HIV disease, this indication is based on the results from a study that showed a reduction in both mortality and AIDS-defining clinical events for patients who received Norvir. Median duration of follow-up in this study was six months. The clinical benefit from Norvir therapy for longer periods of treatment is unknown. For patients with less advanced disease, this indication is based on changes is surrogate markers in studies evaluating patients who received Norvir alone or in combination with other antiretroviral agents.

Marijuana is approved for medical use:

Ballot measures in the states of California and Arizona were passed in late 1996 legalizing the drug for certain medical uses. It is still uncertain how the mandates will be implemented by law enforcement. The potential problem with these state mandates is that they conflict with federal laws, that still prohibits the use of marijuana. Physicians may still be arrested for prescribing it, because the federal government issues drug permits to doctors and federal law still prohibits the prescription of marijuana. Army Gen. Barry McCaffrey, director of President Clinton's national drug control policy and an outspoken critic of the proposition, said he plans to meet with Attorney General Janet Reno and other US government officials to discuss how federal law should be enforced in these cases. We will update this topic as these updates become available.

Amprenavir

Amprenavir is the fifth HIV protease inhibitor marketed. Indicated in combination with other antiretroviral drugs for treatment of HIV-1 infection, amprenavir (Agenerase, Glaxo Wellcome; Vertex) joins four other HIV protease inhibitors: indinavir, nelfinavir, ritonavir, and saquinavir.

How amprenavir compares with other drugs in its class is still under study. However, preliminary data suggest that it has a different resistance profile than other protease inhibitors and may be effective against some HIV strains that have become resistant to other drugs. It can be used to treat children as young as age four; its safety and effectiveness in younger children haven't been established.

Like ritonavir, amprenavir is administered only twice a day (three times a day is currently recommended for the other three protease inhibitors). However, the patient must take eight capsules of amprenavir per dose, a disadvantage for the new drug.

Precautions:

(1) Use is best avoided in patients who are hypersensitive to sulfonamides; amprenavir is a sulfonamide. Closely monitor any patient undergoing concurrent therapy with a sulfonamide-containing product such as trimethoprim-sulfamethoxazole (Bactrim), which is commonly prescribed to prevent or treat HIV-related respiratory infections.
(2) Contraindicated for concurrent use with bepridil, cisapride, dihydroergotamine, ergotamine, midazolam, and triazolam. Amprenavir may inhibit the metabolism of these drugs, dangerously increasing their activity.
(3) Use cautiously with amiodarone, lidocaine, quinidine, tricyclic antidepressants, and warfarin, and closely monitor serum concentrations (or, in the case of warfarin, the international normalized ratio) throughout therapy.
(4) Amprenavir may increase the activity and risk of adverse effects of lovastatin, simvastatin, rifabutin, sildenafil (Viagra) and reduce the effectiveness of hormonal contraceptives. Many other common drugs, such as rifampin (Rifadin), phenobarbital, phenytoin, and antacids, can reduce amprenavir's effectiveness. Consult the product labeling for a listing of possible drug interactions, precautions, and recommendations. (5) Reduce the dosage in patients with impaired liver function. (6) Closely monitor patients with hemophilia for spontaneous bleeding.

Adverse reactions (when used in combination with zidovudine and lamivudine): nausea; vomiting; taste disorders; paresthesia (oral, perioral, or peripheral); depressive or mood disorders; mild or moderate rash; hyperglycemia, new-onset diabetes mellitus or exacerbation of preexisting diabetes mellitus; redistribution or accumulation of fat, including central obesity, dorsocervical fat enlargement (buffalo hump), peripheral wasting, breast enlargement, and cushingoid appearance; severe or life-threatening rash, such as Stevens-Johnson syndrome (rare)

Nursing considerations:

(1) The liquid formulation is 140 less bioavailable than the capsule formulation, so the formulations aren't interchangeable on a milligram-per-milligram basis.

(2) Tell the patient that he can take amprenavir with or without food, but that he should avoid taking it with a high-fat meal.

(3) Warn him not to take vitamin E supplements: Amprenavir contains vitamin E in an amount that far exceeds the daily recommended allowance. Excess vitamin E may exacerbate vitamin K deficiencies caused by anticoagulant therapy or malabsorption, leading to bleeding problems.

(4) Warn women of childbearing potential that amprenavir may lessen the effectiveness of hormonal contraceptives; recommend alternative or additional barrier contraceptives. .

(5) Advise men who also take sildenafil that they're at increased risk for such adverse effects as hypotension, visual changes, and priapism.

(6) If the patient misses an amprenavir dose by more than four hours, tell him to wait and take the next dose at the regularly scheduled time. If he misses the dose by fewer than four hours, tell him to take the missed dose immediately and the next dose at the regularly scheduled time.

(7) If he uses an antacid, instruct him to separate the antacid and amprenavir by at least one hour.

DRUG THERAPY AND THE ELDERLY:

The normal aging process causes changes to occur in the elderly which will affect the way drugs are absorbed and utilized in the body. If you consider this fact along with the fact that as the person gets older, compliance with drug regimens also occurs. Drug-Drug interactions also can occur when the elderly are taking multiple drug therapies.

Some specific alterations that occur are as follows:

1. Altered absorption:

The main factors that affect drug therapy in the elderly are the decreased gastric emptying time, combined with a rise in gastric juices. This factor alone can cause irritation to the stomach mucus membrane in addition to decreased absorption of some drugs.

2. Altered distribution:

Distribution of some drugs may be affected by the aging process. With age, the distribution of fat tissue in the body is changed. Fat tissue tends to increase in mass as compared to the entire body mass. As a result, the fat soluble drugs can be retained in these tissues and build up to the point of toxicity. Some of these fat soluble drugs are: the phenothiazines (Thorazine, Vesprin, Mellaril) and the benzodiazepines (Valium). This condition may also cause certain water soluble drugs to build up toxic levels quickly at normal doses, due to reduced body fluids in old age.

Distribution of some drugs is also affected by the chronic illnesses of old age. Chronic illness and poor nutrition can often lower the body's serum protein (albumin) levels. This lowered serum albumin can increase the free amount of certain drugs in the blood; and hence the concentration is increased and toxicity may increase.

3. Altered metabolism:

In this category, the liver is the main focus of attention. With aging, the liver function declines. Enzyme production decreases and blood flow through the liver decreases as well. These factors cause certain drugs to not be metabolized as quickly as they should be. Therefore, certain drugs will have a greater concentration in the plasma and tissues because the liver is not getting rid of the drug as it normally should--an increase in the halflife of the drug. Over time, these factors can lead to drug toxicity. The drugs most affected by this condition of aging are: propranolol (Inderal), lidocaine (Xylocaine), and narcotic analgesics (meperidine [Demerol], morphine).

4. Altered excretion:

Some drugs are removed from the body through the excretory system. In aging, there is diminished renal blood flow, diminished glomerular filtration rate, tubular secretion, and reabsorption. these factors can lead to drug toxicity from lack of excretion of certain drugs (or their metabolites). Drugs in this category include: Aminoglycosides, lithium carbonate (Lithuania, Lithonate), furosemide (Lasix), and Digoxin.

Calcium and the Elderly:

The importance of calcium in the diet is well recognized. Calcium is required for: neurotransmitter storage, nerve impulse transmission, muscle contraction, including cardiac contraction/conduction, cell membrane permeability, blood clotting, renal function, hormone storage and release, and other functions. In 1984, the National Institute of Health panel recommended that postmenopausal women and elderly persons increase intake of calcium to 1,500 mg. However, this amount of calcium is generally thought to be excessive, according to most nutrition experts. Recommended Dietary Allowance (RDA), of calcium for adults is 800 mg/day.

Elderly persons tend to absorb calcium inefficiently, the increased gastric acid secretion during meals may improve tablet dissolution. Therefore, the elderly should not take calcium tablets during meals, as would the "normal" adult. Also, calcium taken with meals will tend to interfere with the absorption of iron supplements which are also usually taken with meals. Therefore, the optimal time for calcium supplements for the elderly, would be in between meals. Calcium tablets in between meals should be taken with an 8-ounce glass of water or juice in order to help promote absorption. Calcium citrate and Calcium lactate are preferable for their solubility (Todd 1989). These two preparations are generally more readily absorbed than other calcium preparations.

The side effects of calcium supplements in the elderly are generally not serious. They include: constipation, flatulence, and rebound gastric acidity. Calcium supplements in the elderly may also lower the blood pressure in calcium-deficient hypertensive patients. The more serious side effects are usually only seen with chronic use of these supplements in doses above 1,500 mg per day and with concurrent vitamin D supplementation. Supplements in the elderly should be monitored carefully. Doses of calcium should not exceed the 1,500 mg per day. Levels above this tend to be non-beneficial; in fact, high doses of calcium have been shown to actually block absorption into bone. Signs and symptoms of hypercalcemia include: anorexia, dry mouth, metallic taste, nausea, vomiting, severe constipation, headache, drowsiness, mental depression, irritability, confusion, muscle or bone pain, polyuria, hypertension, bradycardia, or arrhythmias.

CONDITIONS UNDER WHICH THE NEED FOR CALCIUM RISES:

1. When the diet has:

High Fat, High protein, High sodium, High Sugar, High phosphate, High vit D, inadequate vitamin D

2. When Physical Conditions Include:
Cushing's syndrome, hypopituitarism, hysterectomy, thyrotoxicosis, oophorectomy

3. When Patient takes such drugs as: alcohol, aluminum antacids, caffeine, cholestramine, Corticosteriods, antineoplastics, furosemide, heparin, phenobarbital, phenytoin, thyroid hormone, tobacco

4. When the patient is immobile or sedentary.

Drugs and the Elderly: Do You Know the Risks? (Lee)

Adverse effects from medications take a heavy toll on older people. Learn how age-related physiologic changes, health problems, and polypharmacy can put your patients at risk for harmful drug reactions--and how you can help reduce the danger.

When 86-year-old Gladys Martin didn't answer the phone one morning, her daughter became alarmed and decided to drive over to the senior citizen complex where Ms. Martin lived. As she let herself into the apartment, she heard faint crying from the direction of the bathroom, where she found her mother on the floor, unable to move.

An ambulance brought Ms. Martin to a local hospital emergency department, where X-rays revealed that she'd broken her hip. When a nurse asked her what happened, Ms. Martin explained that she had felt groggy and confused that morning and was having trouble walking. When she went into the bathroom, she said, her legs gave way.

On further questioning, Ms. Martin mentioned that she'd taken diazepam (Valium) to help her sleep the previous evening, and that she regularly took diltiazem (Cardizem) for hypertension and cimetidine (Tagamet HB) for heartburn. At that point the nurse realized Ms. Martin had probably been affected by a "sedative hangover" that morning, since cimetidine tends to slow the hepatic metabolism of diazepam.

Stories like Gladys Martin's are all too common. One study has found that adverse drug reactions contribute to one in 10 hospital admissions of older persons. The toll of harmful drug side effects is expected to grow in the years to come as the nation's population ages.

There are several reasons for older adults' greater susceptibility to adverse drug reactions. Even healthy older bodies generally don't metabolize and eliminate drugs as effectively as younger ones. Age is also associated with health problems that impair the body's handling of drugs and its ability to tolerate both therapeutic and toxic effects.

And older people take more medicine. One study, in fact, found that older patients were taking an average of eight different prescription or over-the-counter drugs a day. The more drugs a person takes, the greater the risk of harmful drug interactions as well as adverse effects from individual drugs. Unfortunately, physicians often prescribe drugs without ascertaining what medications the patient is already taking and making necessary adjustments to minimize interaction risk. In addition, some patients take drugs that are less desirable for older people than other medication options because of adverse effects or lack of efficacy.

It's easy to miss adverse drug reactions, because many such reactions, as confusion, dizziness, fatigue, or constipation, are common, nonspecific symptoms frequently encountered in geriatrics. That makes it more important to keep in mind the possibility of adverse reactions in older patients.

Here I'll review how age-related physiologic changes alter pharmacokinetics, or how the body acts on drugs. I'll explain how these changes can make many frequently prescribed drugs and combinations of drugs more hazardous for the older patient. And I'll suggest steps you and others on the care team can take to identify and safeguard patients at risk.

Drug interactions that slow absorption

Although aging brings various changes in gastrointestinal (GI) tract function (increased gastric pH, decreased gastric emptying, impaired intestinal motility, and reduced splanchnic circulation), these alone don't ordinarily alter drug absorption enough to necessitate avoiding a medication or adjusting its dosage.

However, certain conditions common in older people, such as diarrhea, achlorhydria or malabsorption, can combine with these basic physiologic changes to reduce absorption significantly. The usual dose of a drug may not produce the expected therapeutic effect, and a higher dose may be required.

A more common concern is the use of combinations of drugs in which one drug may affect absorption of another. For example, antacids contain calcium, magnesium, or aluminum ions that can bind to many other drugs, forming insoluble, nonabsorbable complexes that pass out of the body in feces. Almost always, there's a decrease in the therapeutic effect of the other, "object" drug. Among the drugs affected in this way by antacids are quinolones (ciprofloxacin, norfloxacin, ofloxacin [Floxin]), tetracyclines, iron salts (such as ferrous sulfate), ketoconazole (Nizoral), and isoniazid (Nydrazid).

To avoid such problems, recommend that the patient take the object drug at least two hours before taking the antacid. This will allow adequate absorption of the object drug before the antacid reaches the GI tract. Or advise the patient to take the object drug several hours after taking the antacid, which will allow enough time for gastric emptying of the antacid.

Free to cause trouble

Once they are absorbed and enter the circulation, many drugs bind to proteins. In the bloodstream, an equilibrium is maintained between protein-bound and unbound or free fractions of drug, with proportions varying with the drug. The free fraction of drug exerts therapeutic and toxic effects, while bound drug is inactive until released from the protein.

Albumin is the principal circulating protein to which drugs bind. Since production of albumin by the liver generally declines with age, there is an age-related rise in the free fraction of highly protein-bound drugs. This change alone isn't clinically significant, but when the individual also has an illness that reduces drug binding to albumin, free drug concentrations may be high enough to cause adverse drug reactions or interactions. Medical conditions can reduce protein binding of drugs by:

- decreasing albumin production (malnutrition, cancer, and liver disease)
- reducing drug binding affinity to albumin (hyperbilirubinemia, diabetes, uremia)
- increasing albumin catabolism or excretion (nephrotic syndrome, surgery, burns, or protein-losing enteropathy)

Clinical effects from lessened drug binding to albumin are most likely to occur with agents that are at least 90% protein-bound. At **any given time** 100 or less of such a drug will be free and active. Even a small drop in plasma levels of albumin can result in a large increase in unbound drug.

One such medication is phenytoin (Dilantin). Older patients taking phenytoin who develop an illness that reduces plasma albumin levels will attain higher concentrations of unbound drug with their usual daily doses. The 300 mg per day dose commonly used in younger, healthy patients may produce such effects as sleepiness, confusion, nystagmus, diplopia, or ataxia in a geriatric patient with hypoalbuminemia.

Besides assessing the patient for these signs and symptoms, be sure to monitor free phenytoin serum concentrations. Routine phenytoin blood testing typically only provides the total concentration, so you should discuss with the physician the possibility of obtaining measurements of unbound concentrations as well. This will allow you to monitor concentrations of active drug and detect any correlation between concentrations and symptoms. Therapeutic total serum phenytoin concentration normally ranges from 10 to 20 mg/dL, so therapeutic free concentration ranges from 1 to 2 mg/dL. If you note an elevation in free concentrations, notify physician so he can adjust dosage.

The anticoagulant warfarin (Coumadin) is even more highly protein bound--normally 99%. Any increase in the unbound fraction can raise the risk of excessive anticoagulation and bleeding complications. Older patients who have conditions known to reduce albumin serum concentration or drug binding to albumin warrant close watch for warfarin toxicity. In assessing such patients, ask about and look for such signs and symptoms as heavy bleeding from cuts or wounds, bleeding from the gums or nose, unexplained hematomas or ecchymoses, hematuria, hematemesis, or black, tarry, or bloody stools.

Patients who start on warfarin or whose dosage is adjusted should have regularly scheduled anticoagulation testing- -prothrombin time (PT) or the international normalized ratio (INR)--until the results indicate stable anticoagulation. If an underlying medical condition associated with low albumin serum concentrations worsens, it may be necessary to retitrate the patient's dose of warfarin.

Other drugs that are normally highly protein-bound include aspirin, diflunisal (Dolobid), naproxen (Naprosyn, Anaprox), tolbutamide (Orinase), and valproate (Depakene). When any of these drugs is used in an older patient, it's advisable to start with the lowest effective dose and to increase the dose slowly and carefully to avoid adverse effects.

Causes of Impaired Hepatic Metabolism:

Conditions:

cirrhosis cancer with liver metastasis heart failure fever malnutrition thyroid disease (by decreasing blood flow to the liver) **Drugs:**

allopurinol (Zyloprim) cimetidine (Tagamet) ciprofloxacin (Cipro) diltiazem (Cardizem) enoxacin (Penetrex) fluconazole (Diflucan) isoniazid (Nydrazid) ketoconazole (Nizoral) metronidazole (Flagyl) ranitidine (Zantac) trimethoprim-sulfamethoxazole (Bactrim, Septra) verapamil (Calan, Isoptin) **Slowed metabolism in the liver:**

With age, the mass of functional liver tissue diminishes and blood flow to the liver decreases. Consequently, the capacity of the liver to catabolize drugs and their metabolites declines. Also, hepatic microsomal enzymes responsible for oxidizing and reducing drugs act more slowly, so a drug or active metabolites may remain in the body longer. Although this may not present a problem if a drug is taken on an as-needed basis, repeated dosing may result in significant accumulation of the drug--and possibly greater risk of toxicity.

Also, various medical conditions more common in older adults can impair liver function directly by further reducing metabolic activity or indirectly by decreasing hepatic blood flow. And certain commonly prescribed drugs, even in usual doses, can slow drug metabolism.

When an older patient whose hepatic metabolism may be slowed due to illness or medication is prescribed a new drug, determine whether that drug is metabolized in the liver. The prescribing information will usually indicate this. or, you can ask the pharmacist. If a drug does undergo significant hepatic metabolism, it may be prudent to reduce the dose or lengthen the dosing interval, and you may want to discuss that possibility with the prescribing clinician.

Also, monitor the patient for adverse reactions that can result from slowed drug catabolism. These will usually appear within several days to a week after the drug is begun. If they do occur, the drug should be stopped at least temporarily. If therapy is to be resumed, the prescribing clinician should consider lowering the dose or lengthening the interval between doses.

In some cases, a drug that doesn't require hepatic metabolism to be excreted may offer an alternative. For example, a patient with hypertension and liver dysfunction who needs a beta-blocker could be treated more safely with nadolol (Corgard), which isn't metabolized by the liver but is excreted unchanged by the kidneys.

When benzodiazepines linger too long:

Long-acting benzodiazepines--diazepam (Valium), chlordiazepoxide (Librium), and flurazepam (Dalmane)--all have long plasma half-lives and rely on the hepatic microsomal enzyme system for breakdown into metabolites, which are eventually excreted by the kidney. In older patients, these drugs will remain in the body longer, and with repeated administration they can cause unwanted daytime sedation or lethargy in the morning. Excessive sedation can result in dizziness and even falls, as happened with Ms. Martin.

Intermediate- or short-acting antianxiety agents can help minimize this risk. Their hepatic metabolism is slowed only slightly with age, and their duration of action is similar in young and old adults. Examples of such agents include the short or intermediate-acting benzodiazepines lorazepam (Ativan), temazepam (Restoril), triazolam (Halcion), alprazolam (Xanax), and oxazepam (Serax), and such nonbenzodiazepine sedatives as zolpidem (Ambien) and buspirone (BuSpar).

Long-acting benzodiazepines and cimetidine (Tagamet) can be a particularly risky combination in older people, as Ms. Martin's accident demonstrates. Cimetidine inhibits the hepatic microsomal enzymes that break down long-acting benzodiazepines and so may prolong the drugs' duration of action. This may cause oversedation, confusion, or ataxia. If you encounter an older patient taking cimetidine and long-acting benzodiazepines, bring this to the attention of the prescribing clinician. The patient can be switched to a shorter-acting benzodiazepine or to a different antiulcer medication, such as famotidine (Pepcid) or nizatidine (Axid), that doesn't inhibit the hepatic microsomal enzyme system.

Adverse Effects of Drugs Metabolized by the Liver:

Drug Signs and symptoms of excessive drug effects: caffeine: nervousness, jitteriness, anxiety, insomnia; **carbamazepine (Tegretol):** dizziness, drowsiness, blurred vision, **ataxia; long-acting benzodiazepines: diazepam (Valium), flurazepam (Dalmane), chlordiazepoxide (Librium):** sleepiness, daytime hangover-like effects, confusion, dizziness, loss of memory; **lidocaine (Xylocaine):** dizziness, confusion, blurred vision, seizures, decreased heart rate; **theophylline (Theo-Dur, Slo-Phyllin):** nausea, vomiting, palpitations, racing pulse, convulsions, nervousness; **narcotic analgesics, such as morphine, meperidine, and hydromorphone (Dilaudid):** sleepiness, respiratory depression; **warfarin:** increased bleeding, unexplained bruising, prolonged prothrombin time (PT) or high international normalized ratio (INR); **oral hypoglycemic agents, including tolbutamide (Orinase), glipizide (Glucotrol), and glyburide:** dizziness, headache, nausea, vomiting, sweating, palpitations; **phenytoin:** sleepiness, confusion, blurred vision, ataxia, liver enzyme elevations; **antihistamines, such as Benadryl and Seldane:** dry mouth, confusion, sedation, palpitations, constipation, urine retention; **beta-adrenergic blocking agents, such as propranolol:** hypotension, slowed pulse rate, slowed heart rate.

Renal function decline; Calculating the risk:

Renal function declines with age. This can be seen in measurements of creatinine clearance, which reflect the filtration and excretory capacities of the nephrons in the kidneys. Normal creatinine clearance in a young adult is 100 to 120 mL/minute. But after age 40, creatinine clearance falls by 10% for every decade of life. A 70-year-old will typically have a creatinine clearance of about 70 mL/minute. Many illnesses more common in older patients--diabetes, hypertension, heart failure--can compound age-related loss of renal function and so further reduce creatinine clearance.

When creatinine clearance falls below 30 mL/minute, the excretion of drugs that are eliminated mainly by the kidneys decreases significantly--and the risk of accumulation of the drug and metabolites increases. What's more, if the drug is potentially nephrotoxic, the danger of injury to the kidneys increases with the degree of impairment of renal function.

Fortunately, a healthy patient's level of renal function can be estimated using simple formulas that calculate creatinine clearance from serum creatinine level, age, and weight:

For men, the formula is:

Creatinine clearance (mL/minute)=
(140 - age) x weight (kg) 4 (serum creatinine [mg/dL] x 72)

For women, the formula is:

Creatinine clearance (mL/minute) _
0.85 x (140 - age) x weight (kg) 4 (serum creatinine [mg/dL] x 72)

These formulas accurately estimate creatinine clearance in patients who are at least five feet tall, aren't obese, have stable renal function (meaning serum creatinine concentration doesn't fluctuate by more than 0.4 mg/dL with each measurement), and have no severe muscle wasting. If your patient doesn't meet these criteria, consult a physician or pharmacist, who may know other formulas for assessing renal function.

If calculations indicate that a patient has below-normal renal function (creatinine clearance less than 100 mL/minute), it's important to determine whether the dosing regimen of any newly prescribed drug should be modified (see When to Adjust for Renal Impairment). A pharmacist can advise you.

When to Adjust for Renal Impairment:

The following drugs require dosage adjustment for patients with diminished renal function:
allopurinol (Zyloprim)
aminoglycoside antibiotics:

- mikacin (Amikin)
- gentamicin (Garamycin)
- netilmicin (Netromycin)
- tobramycin (Nebcin)> atenolol (Tenormin)

chlorpropamide (Diabinese) cisplatin (Platinol) digoxin (Lanoxin) histamine-2 receptor antagonists:

- cimetidine (Tagamet)
- famotidine (Pepcid)
- nizatidine (Axid)
- ranitidine (Zantac)

lidocaine (Xylocaine) lithium carbonate (Eskalith, Lithobid, Lithotab) methotrexate (Folex) nadolol (Corgard) nitrofurantoin (Furadantin) plicamycin (Mithracin) sulfonamides, such as trimethoprim-sulfamethoxazole (Bactrim, Septra) vancomycin (Vancocin)

The hazards of aminoglycosides:

Aminoglycoside antibiotics--amikacin (Amikin), gentamicin (Garamycin), netilmicin (Netromycin), and tobramycin (Nebcin)--rely totally on the kidneys for excretion and can be dangerous for older persons with reduced renal function. When treatment requires multiple doses, older patients generally will receive smaller doses of these agents.

When the serum concentration of any of these drugs is persistently elevated, which is more likely in patients with preexisting renal impairment, acute renal failure may occur after as little as a week of continuous treatment. The risk is greater when trough serum levels of the drug (the lowest levels, measured just before the next dose) are high. Fortunately, nephrotoxicity can usually be reversed by stopping the drug.

Two other possible toxic effects of aminoglycosides--hearing loss and balance disturbances--are often irreversible. The cochlear and vestibular systems in the ears, which are responsible for hearing and balance, respectively, are sensitive to elevated levels of the drugs. Ototoxicity has been correlated with high peak as well as high trough serum drug levels.

Monitoring of serum drug levels is indicated in the patient with impaired renal function if aminoglycoside therapy lasts more than three days. When the drug is administered IV, blood for trough level measurement should be drawn within 30 minutes before administration of the next dose; for peak measurement, the sample should be drawn within 30 minutes after the end of the infusion. Immediately notify the physician of elevated levels (safe levels are generally cited in the product labeling).

Serum creatinine should also be measured daily or at least every other day during prolonged courses of aminoglycosides, and creatinine clearance should be recalculated. If there are any changes in renal function, the dose should be adjusted accordingly. In addition, it's important to ensure adequate hydration. Aminoglycosides and loop diuretics, such as furosemide (Lasix) and ethacrynic acid (Edecrin), need to be coadministered with caution.

The synthetic opioid analgesic meperidine (Demerol) is another drug that poses risks to older patients with renal impairment. Actually, toxicity is caused by an active metabolite, normeperidine, which is eliminated by the kidneys. Normeperidine has a long half-life--five to 20 hours in healthy, young adults, even longer in older patients. While it has less analgesic effect than the parent drug, the metabolite is neurotoxic. When an older patient receives repeated doses of the drug, the metabolite may accumulate faster than it can be excreted. High blood concentrations can lead to seizures and convulsions.

For the older patient with severe pain, other narcotic analgesics that don't rely on the kidney for elimination, such as morphine or hydromorphone (Dilaudid), are safer choices. They may also be more effective, since a dose of meperidine provides pain relief for only about three hours.

Altered end-organ effects:

Changes in the way a drug acts on the body--its pharmacodynamics--may occur with aging. It's difficult to distinguish the contribution of such effects to altered response from that of pharmacokinetic changes, and there's less information about them.

Pharmacodynamic changes may affect organ systems that aren't intended targets of a drug. For reasons unknown, older adults appear to be more sensitive to anticholinergic adverse drug reactions. These effects result from inhibition of the parasympathetic nervous system due to blockade of nerve receptors for acetylcholine. Such reactions, which include blurred vision, confusion, disorientation, dry mouth, dry eyes, constipation, palpitations, worsening of glaucoma, and urinary retention, can be extremely uncomfortable and even dangerous and so may require discontinuing therapy. Anticholinergic effects are common with certain antipsychotic agents, tricyclic antidepressants, and antiparkinson drugs.

Among patients at particularly high risk for anticholinergic drug effects are men with prostatism. Anticholinergic agents block contraction of the detrusor muscle, which is responsible for squeezing urine out of the bladder. Men with prostatism, whose urinary flow is already compromised, may experience acute urinary retention with the drugs. And in patients with narrow-angle glaucoma, anticholinergic agents will block the exit of aqueous humor from the anterior chamber of the eye, increasing intraocular pressure and worsening retinal damage.

Such high-risk patients and others who experience anticholinergic effects can often be prescribed drugs that are less likely to cause such effects (see Minimizing Anticholinergic Effects). When assessing a patient who has been prescribed a drug with possible anticholinergic effects, ask about these effects, and if the patient reports any, inform the physician and document having done so.

Monitor the patient carefully

An important aspect of your role in safeguarding patients from adverse drug reactions is careful monitoring. When a patient is prescribed a new drug, make sure you're familiar with its possible adverse effects. Note also what laboratory tests are important in detecting toxicity. Include evaluation for symptoms or signs of excessive therapeutic effect or other adverse reactions in your assessments. Monitor patient all the more closely if he/she has several conditions requiring drug therapy or has impaired renal function or any other medical problem that affects how the body handles drugs.

When a patient develops a problem after starting a drug, always consider the possibility that the problem could be related to the drug. At the first sign of a possible adverse drug reaction, notify the physician and document your findings and action. In many cases, dose reductions or other simple modifications can significantly improve the patient's tolerance to a drug without compromising the therapeutic benefit.

Uncovering dangers through a drug history:

You can also help prevent adverse drug reactions by taking a careful drug history from the patient. If possible, physically examine the patient's medications. The patient may not remember all the medications he/she takes, their names, and their dosages. Ask the patient's spouse or other family member to bring to the hospital any medications, prescription or nonprescription, that the patient didn't bring with. her when admitted.

For each medication, find out:

- who prescribed it and why
- what dosing instructions the patient was given (such as how many times a day to take it, when to take it, and if the drug should be taken with meals) and whether he/she has followed them
- whether the patient has followed any instructions on avoiding foods that may interact with the drug (for example, abstaining from leafy vegetables containing vitamin K, such as spinach, if she's taking warfarin)
- whether the patient feels that the drug has helped
- any adverse effects (you may need to review the common adverse effects listed in the prescribing information first).

Chart your findings in the nursing admission history record.

For each nonprescription drug, ask the patient:

- why he/she takes it and how often
- whether he/she believes it helps
- who recommended the drug
- whether the physician knows he/she takes it

Also, ask about use of alternative medicines and recreational drugs such as alcohol. Again, document your findings.

A common problem your history may uncover is use of multiple medications, with the potential for harmful interactions or additive side effects. Polypharmacy can easily occur when a patient has seen several physicians for separate health problems and has been prescribed different medications by each. One or more physicians may fail to ask the patient about medications prescribed by others. A patient's cardiologist may prescribe an antianginal drug without knowing what a rheumatologist has prescribed for arthritis. To make matters worse, the patient may have different prescriptions filled at different pharmacies, so individual pharmacists won't know the patient's medication profile and will miss the potential for interactions. Over-the-counter drugs compound the likelihood of drug interactions.

You may also find that the patient has been prescribed a drug that by itself may be unsafe. A 1994 study found that nearly a quarter of adults over 65 living in the community had been prescribed drugs that a consensus panel judged inappropriate for older patients due to adverse drug reaction risk or lack of efficacy. The most commonly prescribed drugs included the antiplatelet agent dipyridamole (Persantine), the analgesic propoxyphene (Darvon), and the antihypertensive propanolol (Inderal).

Following up on your findings:

In speaking with the physician, stress your common concern for the patient's safety. Be prepared to explain why you think a drug or combination of drugs is risky. Cite specific possible adverse effects and interactions as noted in drug labeling and other literature. Point out information in the patient's chart, such as assessment findings or laboratory test results', that supports your position.

A geriatric clinical specialist or nurse practitioner, if available, can also help you assess the risks to the patient and determine how the risks might be prevented or managed.

In addition, consult with a pharmacist. These professionals have been educated about proper drug use, identifying and preventing adverse drug reactions, and adjusting drug doses in the face of impaired hepatic metabolism or renal function. Of course, a pharmacist may identify problems by reviewing medication orders or the patient's drug profile.

Teaching the patient to take medicines safely:

The patient him/herself has an important part to play in avoiding adverse drug reactions. Adherence to prescribed therapy--taking the right dose of the right medication at the right time--helps prevent problems. But the patient can't follow a medication regimen if she doesn't understand it.

What a patient needs to know about medication varies with the drug, but some essentials include:

- the brand and generic names of the drug and why it has been prescribed
- the form and appearance of the drug
- how often and when it should be taken and should it be taken with meals
- whether to avoid alcoholic beverages or any foods
- what, if any, over-the-counter drugs to avoid
- side effects to watch for
- when to call the physician if adverse effects develop

To verify that the patient understands her regimen, ask her to recall immediately and again later during her hospital stay what you have told her. Written materials, which the pharmacy may provide in the form of printouts from the hospital computer system, help reinforce your instructions.

Especially if the patient's medication regimens are complicated or if she's cognitively impaired, encourage the spouse or another family member to be present for your instruction. Review the guidelines with the patient and family just prior to discharge, and if possible provide a written medication schedule for the patient to follow at home.

Medications help older people to overcome life-threatening acute illnesses and to live successfully with chronic diseases. But with the benefits can come risks. By knowing what drugs your patient is taking and their potential dangers, watching carefully for untoward effects, communicating your concerns to colleagues, and taking the time to teach, you can help the older adult get the better part of the medication bargain.

Undesirable Drugs for Older Patients:

Drug Problem: Long-acting benzodiazepines: diazepam (Valium), chlordiazepoxide (Librium), flurazepam: produce daytime hangover-like effect due to prolonged duration of action; shorter-acting benzodiazepines are considered safer meprobamate accumulates with repeated dosing; **pentobarbital, secobarbital (Seconal) accumulate with repeated dosing; amitriptyline (Elavil):** has potent anticholinergic side effects; **indomethacin (Indocin):** headaches are more common than with other nonsteroidal anti-inflammatory agents; may also worsen depression; **chlorpropamide (Diabinese):** causes prolonged hypoglycemia; **propoxyphene (Darvon) metabolite, norpropoxyphene,** can cause arrhythmias, particularly in patients with impaired renal function **pentazocine (Talwin):** can cause seizures, hallucinations, or arrhythmias when taken in large doses; **Vasodilan:** ineffective as dementia treatment; **Muscle relaxants: cyclobenzaprine (Flexeril), orphenadrine (Norflex), methocarbamol (Robaxin), carisoprodol (Soma):** potential for central nervous system toxicity is greater than potential benefit; **trimethobenzamide (Tigan):** less effective than alternative agents; may cause drowsiness and other adverse effects **dipyridamole (Persantine):** efficacy unproven.

DRUG INTERACTIONS:

If you **take**	**Then Adding calcium can**
1. etidronate (Didronel):	decrease absorption of iron
2. tetracycline:	decrease absorption of oral tetracycline
3, thiazide diuretics:	increase calcium blood level
4. magnesium-containing meds:	increase magnesium blood level
5. phenytoin:	decrease bioavailability of both drugs
6. Potassium phosphates (Neutra-phos):	increase potential for calcium deposits in soft tissues
7. Veraoamil (Calan, Isoptin):	antagonism of Verapamil effect

Pharmacodynamic Changes in Aging

Pharmacodynamics refers to the actual effects of drugs on a target site. Although studied less extensively in the elderly than pharmacokinetics, altered pharmacodynamic responses at the target organ may be anticipated with aging. Some pharmacologists believe that the exaggerated responses to drugs in the elderly, rather than being a result of altered pharmacodynamic interactions, are actually a result of altered pharmacokinetics or diminished homeostatic responses. These altered responses may be the result of a reduction of neurotransmitter synthesis, the presence of disease states, or other physiologic changes. Age-related changes produce depletions of acetylcholine, dopamine, and serotonin levels; impairment of baroreceptor response to blood pressure changes; and decreased responsiveness to beta-receptor stimulation.

The dose-response relationship of a particular drug is a primary concern in clinical therapeutics. In order to elicit a desired effect with a chemical agent, the relationship between the size of the dose and the intensity of the response to be produced must be known. Age-related changes in target organ sensitivity to drugs may result in an exaggerated response, such as with some sedative-hypnotics and analgesics, or a diminished pharmacologic response, as with beta-blockers and beta agonists, or calcium channel blockers.

Interpatient Variability in Drug Responses

Therapeutic doses can vary significantly among individuals and no two people will respond to the same drug and dose in exactly the same way. Therapeutic dosing levels are determined by drug manufacturers during early phases of experimental clinical trials using animal subjects. Recall, however, that elderly patients are generally excluded from the clinical trials that assist in the establishment of the effective dose. They could receive a standard dose of drug and be receiving either too much or not enough of the drug to be in the therapeutic range. This consideration is most critical when using drugs with a narrow therapeutic index.

Often what determines the effect of drugs, relates to body size and composition, especially the ratio between total body water and fat. In general, drugs exhibit a greater effect in older people because they have less body water.

Patient Factors in Drug Therapy Management

Certain drug self-administration behaviors on the part of the patient may also influence the potential for ADRs. Adherence to the treatment regimen is always a concern with any patient; however, the **elderly may present different challenges** to drug therapy management. As many as 40% of elderly patients do not administer their medications as prescribed, primarily because of the high numbers of drugs prescribed. Most nonadherence is in the form of the patient taking too little of the prescribed medication. Although the elderly may be no less compliant with medication usage than any other age group, special attention should be paid to the frail elderly who may experience greater motor-sensory declines that contribute to an inability to properly take medications.

The primary reasons for nonadherence to drug treatment in the older patient are poor communication with health professionals and declining cognitive function. Other factors contributing to nonadherence include such things as expense of the drug, unsuitable containers, differing and confusing dosing schedules, inadequate understanding of therapy, and forgetting to take the drug in the absence of symptoms. Premature self-discontinuation of a medication is another form of nonadherence. Medication treatment should be reviewed with the patient or family caregiver at each office visit. Reasons for discontinuation or alteration of a prescribed regimen should be thoroughly explored. The discussion may reveal the occurrence of unpleasant adverse effects; inability to afford the drug; complexity of the treatment regimen; physical inability to take the medication, such as swallowing difficulties or osteoarthritis; or confusion about the treatment secondary to drug induced memory loss. It may be helpful to periodically request that the patient bring to the office all of the medication containers he is currently using in order to better assess the actual medications he is taking.

Avoiding ADRs

Prescribing drugs for the elderly patient presents challenges for the primary care provider. ADRs more commonly occur in the elderly and are associated with increased morbidity and mortality. Prevention of ADRs may be improved through careful attention to assessing the need for drug therapy, writing safe prescriptions, monitoring the patient for drug efficacy and adverse events, and educating the patient regarding pertinent signs of adverse reactions. Several key management strategies in drug therapy are suggested to reduce the risk of ADRs and thus increase the potential benefit to the patient.

Assess the need for a drug

- Decide whether the disease or symptoms are worth treating with medications; always weigh risks versus benefits
- Define the goal of drug therapy
- prescriber's goals
- patient's goals
- caregiver's goals.
- Don't attempt to treat an adverse effect from one drug with another drug, unless absolutely necessary
- Review risks of treatment and of potential drug interactions

Write safe prescriptions

- Take a careful drug history--consider that the patient may have more than one provider writing prescriptions and may also be taking OTC agents or consuming alcohol
- Start with the lowest reasonable dose and increase slowly in the attempt to achieve therapeutic goals or levels. Consider the half-life of a drug and possible cumulative effects
- Prescribe only for specific and rational indications; may obtain multiple desired effects from the same drug
- Prescribe the fewest number of drugs possible--keep the dosing regimen simple
- for adverse effects
- Maintain a high index of suspicion for change in cognitive function, affect, or behavior
- Always consider drug treatment as the cause of a change in health sta tus--especially when prescribing newly marketed drugs
- Perform a review of systems with each periodic review of medication treatment and any time new symptoms appear
- Do not assume that a medication once indicated may remain as such. Stop drugs that are no longer needed
- patient education and counseling
- Give the patient a portable prescription record with written descriptions of drug, dosing schedule, and possible adverse effects to report.
- Counsel patient regarding potential drug interactions with OTC medications, alcohol consumption, caffeine, illicit drugs, water, salt, spices, herbs, natural remedies, foods, and beverages
- Inform patient to report any suspected new or unusual symptoms

Conclusion

Avoiding ADRs in the **elderly patient can present the practitioner with** a number of challenges. In order to relieve symptoms and forestall the effects of chronic illness, finding the right combination of agents and dosages requires close attention to detail in monitoring for ADRs. Being aware of the pitfalls of drug prescribing for the elderly and recognizing methods to avoid problems will reduce the likelihood of an adverse outcome.

APPENDIX A

A Drugs withdrawn recently:

1. The thiazolidinedione traglitazone (Rezulin), which was used to treat type 2 diabetes mellitus, has been removed from the market. The FDA requested Warner-Lambert withdraw the drug after higher-than-expected liver damage was reported by patients using the drug.

2. Cisapride (Propulsid) will no longer be marketed in the U.S. It was used to treat gastroesophageal reflux disease but has been associated with 341 reports of arrhythmias, and 80 deaths, as of Dec. 1999. Janssen Pharmaceuticals will continue supplying it through limited access to patients who meet certain specific criteria.

B Pinworms: Common Family Nuisance Easily Treated:

Twice as common as lice, pinworms affect 20-42 million Americans, mostly children; more common in the summer. Pinworm (Enterobius vermicularis) is the most common intestinal worm infection in the U.S., and one of the most common among young children. While it occurs most often in school-age children, pinworm is highly contagious, and can easily spread to the whole family.

Symptoms include severe itching in the anal area, which may lead to fidgeting, irritability, and restlessness. Sleeplessness, bedwetting and even teeth grinding may be signs as well, and excessive scratching may lead to other infections. In girls, pinworms can infect the genital area, causing bladder infection-like symptoms of itching or burning. Because of the low awareness of pinworms, sometimes it is mistaken for other health problems, experts say.

"Because pinworms can cause sleeplessness, and **therefore, concentration** problems, it has been mistaken for attention deficit disorder," says W. Steven Pray, Ph.D., R.Ph. "People aren't aware that there's a nonprescription treatment out there." "When they get a diagnosis, they don't know what to do."

While prescription drugs are available, pinworms are easily treated by over-the-counter medications, such as Pin-X(R) Pinworm Treatment. Pin-X is a'liquid medication taken by mouth and only requires a single dose. It is easily tolerated by children and adults. Because pinworms are highly contagious, it is recommended that all family members and even children's playmates be treated.

Pinworms are small round worms with a white body and pointed tail. During the night, they emerge from the anus to lay microscopic eggs on the surrounding skin, causing swelling and severe itching. Inspecting the anal area at night is the best way to confirm pinworm infection, health experts say.

In his April 1993 article, "Pinworms: A Common Family Nuisance," Dr. Pray recommends finding the pinworms by using a flashlight on the child's anal area an hour or so after the child has gone to bed or applying tape to the rectal area in the morning before the child bathes or uses the toilet. (The highest concentration of eggs are present in the morning.) The tape can be placed in a glass jar or plastic bag and taken to the physician's office to be examined under a microscope.

Sue Partridge, CDC health education specialist, who responds to consumer calls about pinworms, says children become infected by swallowing pinworm eggs, adding that daycare and school-age children are the most susceptible because they haven't learned good hygiene practices. "This can happen through toys, dirty fingers or hand to mouth transfer of eggs," she notes. Because the eggs are easily transmitted, even through the air, pinworms can occur in the cleanest of households.

Appendix B

Culturally Competent Drug Administration (AJN 1999)

"Are one-size-fits-all prescriptions becoming a thing of the past?"

Drug polymorphism: Same Drug, Different Response.

That patients' age, gender, size, and body composition influence their responses to a drug is common knowledge. Such variation in response is called drug polymorphism. What is less widely recognized, however, is that medication administration ought to be determined by ethnicity as well.

Increasingly, studies have confirmed that ethnicity affects how people react to drugs. A Chinese patient may require a lower dose of an antianxiety medication than would a Swedish patient, for example. Or, an African American patient may not respond to an antihypertensive drug like propranolol the way a white patient would. Why the difference?

Factors contributing to drug polymorphism among various ethnic groups can be loosely categorized as environmental, cultural, and genetic. These classifications aren't meant to make generalizations about different ethnicities, nor do they encompass all the factors that may influence a patient's response to a drug; they do serve, however, to raise awareness regarding possible differences in response.

Environmental factors are those that influence the half-life of a drug and its assimilation. Diet, for example, can affect drug absorption. Medications that require fat in order to be absorbed, such as griseofulvin (an antifungal agent) are often more effective in people who maintain a high-fat diet.

Antihypertensive medications also illustrate drug polymorphism: They aren't as effective in people, such as the Japanese, who typically consume diets high in sodium chloride. Malnutrition can influence drug response as well. Protein, vitamin, and mineral deficiencies, which hamper the function of metabolic enzymes, may alter the body's ability to absorb or eliminate a drug.

Smoking, another environmental factor, activates a release of enzymes that tend to accelerate drug metabolism. Stress, physiologic rhythms, and fever also affect drug absorption because they affect the release of hormones and chemicals, such as catecholamines and cortisol, that may either inhibit or accelerate drug metabolism.

In addition, alcohol, which interacts with a number of drugs, including antihypertensives, central nervous system depressants, and antipsychotic agents, may alter a patient's response to medication. Cultural factors, such as values and beliefs, affect drug response as well.

Medication compliance is significantly influenced by a patient's level of education, his prior experience with drug therapy, his expectations regarding the outcome of the therapy, his family's influence on his actions, and his communication with his health care providers. In Japan, for example, nausea, vomiting, and bowel changes related to medication usage are underreported because it's generally not acceptable to complain about gastrointestinal symptoms. A clinician may therefore not be aware that a patient isn't responding well to a particular drug, and will consequently not change the prescription. Or, the patient may stop taking a medication altogether without telling the clinician.

Health care providers should also be aware that, along with prescribed medications, some patients may be taking herbal and homeopathic remedies that can alter response to a particular drug. For example, the Chinese herb ginseng may inhibit or accelerate metabolism, and can therefore significantly affect drug absorption and elimination.

Genetic factors also affect drug efficacy. Because drug metabolism is genetically determined, race may affect response. This is known as genetic polymorphism. Each of us inherits genes that control liver metabolism, which in turn directs the secretion of liver enzymes. Liver metabolism is performed through oxidation and acetylation. People with insufficient metabolism are termed slow or poor metabolizers, while those who metabolize at a faster rate are called rapid or extensive metabolizers.

Three types of genetic polymorphism have been investigated worldwide. Many commonly administered drugs are metabolized via these three pathways.

Acetylation polymorphism was first detected in patients who were treated for tuberculosis with isoniazid. Those who metabolized the drug slowly exhibited elevated serum levels of isoniazid, and were termed slow acetylators. Isoniazid is extensively metabolized in the liver by the metabolic process known as acetylation; this pathway is catalyzed by the enzyme N-acetyl transferase. Slow acetylation often causes elevated drug concentrations, which in turn may lead to increased pharmacologic effects and drug toxicity. Isoniazid has a shorter half-life in rapid acetylators. Patients of European and African descent have been shown to have equal proportions of rapid and slow acetylators among them, but Japanese and Inuit populations have more rapid acetylators than slow acetylators.

The second type, debrisoquine polymorphism, was first recognized in people who are poor metabolizers of debrisoquine, an antihypertensive compound. Extensive metabolizers oxidize the drug faster. Approximately 3o to 90 of whites in the United States, Canada, Britain, Denmark, Sweden, and Switzerland are poor metabolizers of debrisoquine. The Chinese, Japanese, Malaysians, and Thais have the lowest percentage of poor metabolizers, ranging from 01 to 20. Because many commonly prescribed medications including some narcotics, antihypertensives, antipsychotics, and antidepressants, are metabolized similarly to debrisoquine, this polymorphism has extensive clinical significance. For **example, codeine, which is metabolized according** to the debrisoquine pathway, is more likely to be effective in Chinese, Japanese, Malaysian, and Thai patients than in those of European descent. Another example is propranolol, which regulates heart rate and blood pressure better in Chinese men than in white men.

The third type is mephenytoin polymorphism. Mephenytoin, an anticonvulsive agent, is also poorly metabolized in certain patient populations. Various barbiturates and diazepam are metabolized according to the mephenytoin pathway. It has been shown that the percentage of poor metabolizers of mephenytoin is much higher among the Chinese and the Japanese (about 200) than it is in other populations.

Knowledge of genetic polymorphism is most clinically applicable to cases involving drugs that use one of these three pathways, have narrow dosage ranges, and are commonly prescribed. Predictably, it has less clinical application if the dose of a medication is already adjusted to the patient, as is the case with lithium and antihypertensive medications.

Generally, drugs that are titrated for individual tolerance or efficacy simultaneously adjust for race.

Two Well-Researched Drug Classes

Antihypertensives. Because hypertension is more prevalent among blacks than it is among whites, many studies have investigated the effectiveness of the most commonly prescribed medications.

In addition to examining the differences between the drug responses of blacks and whites, researchers have been trying to determine whether these differences are caused by genetics or by the pathophysiology of hypertension. But because most studies have been performed on subjects who already have hypertension, this has been difficult. In 1995, however, Kevin M. Sowinski and colleagues studied the responses to propranolol of healthy black and white subjects, and found that they manifested fewer differences than those who already had hypertension. He concluded that response variations in blacks are most likely caused by hypertensive pathophysiology, which, as subsequent studies have shown, includes decreased renin, increased blood volume, and elevated concentrations of sodium and calcium. Genetically determined differences may indeed exist, but most of them remain unexplained.

Most of the major classes of antihypertensive drugs (diuretics, beta blockers, ACE inhibitors, and calcium channel blockers) are effective in blacks. However, some drugs appear to be more reliable and require lower doses. If only one drug is used, blacks respond better to diuretics than to beta blockers and ACE inhibitors. In addition, within the beta blocker class, labetalol, a combined alpha and beta blocker, has been effective in this population, while propranolol and its derivatives timolol and metoprolol are less so.

Antipsychotic and antianxiety drugs. While it appears that blacks, whites, and Hispanics in the United States require comparable therapeutic doses of antipsychotic, antianxiety, and antidepressant medications, some patients of Asian descent may need lower doses of certain drugs (such as haloperidol) and are therefore more likely to experience adverse outcomes if the drug isn't properly adjusted.

Diazepam, a commonly used antianxiety agent, is metabolized according to the mephenytoin pathway. As mentioned earlier, studies suggest that about 20% of the Chinese and Japanese populations are poor mephenytoin metabolizers. These patients are therefore subject to rapid drug build-up and would require lower doses. one may cautiously conclude that people of Chinese and Japanese descent should be closely observed for sedation, overdosage, and other adverse responses to diazepam.

Different Lands, Different Approaches

Though considering ethnicity when prescribing medications is not **yet common** practice in the United States, other countries have long been doing so. In the U.S., health care emphasizes cure, and prescription practices favor high medication doses with reduced dosing only if the patient experiences adverse effects. American clinicians tend to advocate a one-size-fits-all prescribing approach. Clinicians in European countries, in contrast, prefer adjusting doses upward until the greatest therapeutic value with minimal discomfort is obtained. And in Japan, where patient comfort is emphasized, clinicians prescribe the lowest effective dose to avoid adverse reactions whenever possible. Japanese regulations also mandate that all clinical drug studies be replicated on Japanese subjects, in recognition of the differences in medication response caused by genetic factors.

Though the United States has thus far paid little attention to drug polymorphism caused by cultural and racial differences, it can no longer afford to do so. The ethnic composition of this country is changing rapidly; in 1997, in fact, the Statistical Abstracts of the United States estimated that between the years 2000 and 2010 the number of Hispanics will increase by 31.2%, that of African Americans by 11.60, that of Native Americans by 12.90, and that of Asian Americans and Pacific Islanders by 36.10. The number of whites is expected to increase by 2.70.

These shifts will soon make a uniform approach to prescribing obsolete; it's therefore imperative that clinicians become familiar with the types of drugs that can be affected by a patient's ethnicity.

A Few Roadblocks

A homogeneous study pool. Which is a priority to a drug manufacturer?

Obtaining FDA approval for a new drug, or determining the proposed drug's effectiveness among various patient populations?

Chances are that the former goal takes precedence. Drug trials that select: average patients, mostly white men, are not likely to shed light on the responses of diverse groups to the tested drug. Perhaps drug studies aren't likely to create study pools multiracial enough to answer all of the questions raised by drug polymorphism, but steering away from homogeneity is a start.

HMOs: "If we cover it, we pick it." Managed care providers and HMOs may limit access to practitioners, treatment options, and the range of medications available. A provider's policy may therefore discourage clinicians from prescribing drugs that are deemed too costly, and instead encourage them to administer less expensive ones with similar properties, disregarding important considerations about genetic polymorphism.

Drug derivatives. Most drugs recognized for eliciting varying responses among different ethnic populations have been prescribed long enough to allow opportunities for study. But many of the drugs currently administered are second- or third-generation derivatives of the drugs initially studied. While we may presume that they act similarly, we still don't know the exact pharmacokinetics of specific agents within them.

APPENDIX C

Drug and herbal interactions

Today, more than 60 million people in the United States use herbal and alternative medicines. Herbal drugs are derived from plants, such as gingko biloba, echinacea, and St. John's wort. Alternative drugs are not plant-derived but are outside mainstream pharmacy and include such substances as melatonin, co-enzyme Q-10, shark cartilage, and royal jelly. These agents are being used with increasing frequency by a growing number of patients who, for a variety of reasons, are seeking treatment with largely unproved drugs and therapies. Of greater concern is the fact that nearly three out of four patients who use alternative medicines never mention their use of these agents to their physicians. This sets the stage for potentially dangerous drug interactions. For example, kelp extracts may potentiate the effects of certain anticoagulants and blood pressure drugs. The clinician cannot predict these untoward effects without knowing that the patient is also taking kelp.

Patients should be urged to disclose all drugs they take, alternative or otherwise. Health care providers should routinely include herbal and alternative medicines when asking about their patients' drug use and explain that this information is needed to help prevent or solve problems related to adverse effects or drug interactions. Patients should be told that alternative medicines may be beneficial as well as harmful, but also that they may interact adversely with the patient's prescription medications or could adversely affect that patient's disease.

For their part, clinicians should be informed about the reported uses for complementary and alternative therapies, adverse reactions, and interactions in order to provide effective advice and appropriate cautions to their patients. Echinacea, gingko, ginseng, green tea, kelp, melatonin, and St. John's wort, the substances monographed in this module, are common herbal and alternative drugs that health care professionals may encounter.

The information that follows provides an introduction to potential drug and herbal interactions, and stresses the importance of the clinician's role in monitoring treatment outcomes and preventing dangerous interactions.

(1) St. **John's Wort** has recently been shown to reduce the effectiveness of certain HIV anti-viral drugs. This herbal remedy used to combat depression may also cause heightened sun sensitivity. This herb may also interfere with the absorption of iron and other minerals. Recently, St. John's Wort has also shown to interact with the immunosuppressant cyclosporine. Apparently, St. John's Wort increases the metabolism of cyclosporine, resulting in decreased plasma levels of the immunosuppressant.

(2) Ephedra, used as a decongestant also stimulates the CNS. This should not be used by persons with glaucoma, heart disease, hypertension, or those taking MAO inhibitors.

(3) Ginseng is used to increase energy and alertness. This herb should not be used by persons with cardiovascular disease, diabetes, or glaucoma. It may raise blood pressure and can lower blood sugar levels.

There are many thousands more herbs available today that could have severe interactions with patient's medications. The nurse should always include herbs and home remedies when taking the patient's medication history.

REFERENCES

American Heart Association, Textbook of Advanced Life Support, 2000.

Drug Facts and Comparisons, Facts and Comparisons, Inc., St. Louis, 2000.

Merck Manual of Diagnosis and Therapy, Adverse Drug Reactions, 1999.

Nursing96, Teaching Your Patient About Antidepressants, May 1996.

Nursing2000 Drug Handbook, Springhouse Corp. 2000.

PDR, Physicians Desk Reference, 5411 edition, Medical Economics, N.J., 2000.

The American Academy of Allergy, Asthma, and Immunology, The use of epinephrine in the treatment of anaphylaxis, September 17, 1999.

AJN (American Journal of Nursing), Nurses Drug Watch, AJN, November 2000. AJN (American Journal of Nursing), Nurses Drug Alert, AJN, January 2000. AJN (American Journal of Nursing), Med Errors, AJN, May 2000.

Anderson, J., Allergic reactions to drugs and biological agents, JAMA, 1992.

Bryan, RJ., Administering conscious Sedation: Operational Guidelines, Critical Care Nursing Clinics, University of North Carolina, 1997.

Chodosh, M., et. al., Efficacy and safety of a 10-day course of Grepafloxacin ....., Antimicrobial agents and chemotherapy, January 1998.

Clumeck, N.; Van de Perre, P.; Mascart-Lemone, F.; Cran, S.; Duchateau, J., et al. Dept. of Immunology, St. Pierre Hosp., B-1100 Brussels, Belgium, Int. J. Clin. Pharmacol. Res. 4:459-463 (6) 1994.

Dickens, GR, et. al., Phase I pilot study of the effects of trovafloxacin ...., journal of Clinical Pharmacology, March 1997.

Flynn, CM; Johnson DM; Jones RN., In vitro efficacy of levofloxacin alone or in combination ...., J Chemotherapy, December 1996.

Friend, T., Defusing Dangerous Drug Interactions; USA Today Health., June 6, 1999.

Gleason, Carol, Molle-Matthews, Elizabeth; Emergency Drug Therapy, Nursing Spectrum, 2001.

Goa, KL, et. al., Sparfloxacin ...., Drugs, April 1997.

Goldstein, EJ: Possible role for the new fluoroquinolones in the treatment of anaerobic infections, PDR, Medical Economics Company, 1998.

MO,

Gross, J.B., et al., Practice Guidelines for conscious sedation .... Anesthesiology, 1999.

Hicks, C, Abraham, K., Verapamil and myoclonic dystonia, Anl Itnl Med, 1994.

ISMP, Institute for Safe Medication Practices, Newsletter, Aug, Oct, Nov, Dec 1996.

ISMP, Institute for Safe Medication Practices, Newsletter, Jan, May 1997.

Li, James, Antibiotics: A review of ED use., Emedicine Textbook, Plantz and Adler, eds. 1998.

Lieberman, Anaphylaxis Update; Allergy and Asthma Disease Management Center, October 25, 1999.

Loeb, Stanley, (ed), Nursing 95 Drug Handbook, Springhouse Co., Publisher, 1995 ed.

Ludwig, M., et. A1., Tissue penetration of sparfloxacin ....., Infection, May-June 1997.

McCaffery, M., Pasero, C., Pain: Clinical Manual, St. Louis, Mo., Mosby, 1999.

Morris, Bobbi J., et al., Emergency Contraception, AJN, Sept. 2000.

Raschke, RA, et. A1.; A computer alert system to prevent injury from adverse drug events.., June 5, 1999.

Rodinella, Sandra; and Paquet, Judith; Adverse Drug Reactions, Nursing Spectrum, January 2001.

Russell K Portenoy MD., Taken from March 1986, American Journal of Nursing.

Stroud, Sally, RN; Drug Watch, American Journal of Nursing, Feb 1991 and March 1991.

Talan, D., New concepts in antimicrobial Therapy for Emergency Dept. Infections., Annals of emergency Medicine, 34:4; 1999.

Wroblewski, John; "Terodiline: A New Compound for the treatment of Urge Incontinence," Journal of Ostomy/Wound Management, Sept/Oct 1990.

Yaney, L., intravenous conscious Sedation, Journal of Intravenous Nursing, January 1998.

Yen, Peggy Kloster, Calcium: Taking Mom's Advice; Geriatric Nursing, March/April, 1999.

PHARMACOLOGY UPDATE EXAMINATION BOOKLET - 2001 Edition

Nurses Research Publication for Continuing Education Please read and follow the instructions in the workbook and on the answer sheet. Please send us only the answer sheet (posttest) for grading.

Pharmacology Update PRE-TEST - POST-TEST

Please choose the one best answer for each question. There are no "trick" questions; read each one carefully and refer to the text if you are not sure of the answer. Mark your final answers on answer sheet in pencil.

Chapter I Introduction Pages 7-20

1. You should always when you are giving meds; don't do it out of habit.
A. re-check B. thinkC. wash hands D. call the pharmacy

2. By preventing errors, the nurse will have the opportunity to perform patient:
A. teaching B. supervision C. billing D. procedures

3. GI problems and circulatory problems can interfere with the of the drug.
A. absorption B. penetration C. cost D. distribution E. excretion

4. The fate of the drug refers to the manner in which the drug is:
A. excreted B. absorbed C. distributed D. used by the body

5. "Most Common" gastrointestinal side effects of most drugs include:
A. diarrhea & dystonia C. diarrhea & dysphagia
B. nausea & drowsiness D. nausea & rashes E. diarrhea & constipation

6. An adverse reaction to a drug is an undesirable and usually response.
A. expected B. unanticipated C. mild D. allergic E. fatal

7. is one category of drugs likely to cause allergic reactions.
A. diuretics B. antibiotics C. insulin D. digoxin E. antiemetics

8. Vaccines may cause allergic reactions in those who have sensitivity.
A. antibiotics B. seafood C. egg D. meat E. pork

9. is an acute medical emergency requiring prompt attention.
A. CPR B. drug interaction C. anaphylaxis D. immunologic reaction

10. **Narcotics may cause nonimmunologic reactions, usually those of**
A. hypertension B. anaphylaxis C. urticaria D. bronchospasm

Chapter II Pharmacology Update (Antibiotics) Pages 21-34

11. Zyvox is the first antibiotics in a new class of antibiotics called:
A. penicillins B. flouroqinolones C. antifungals D. oxazolidinones

12. **Lorabid is a broad-spectrum oral antibiotic used to treat infections.**
A. bone B. gastrointestinal C. joint D. skin E. brain

13. **Cefepime is contraindicated in patients who have had immediate hypersensitivity reactions to**

A. erythromycin B. penicillin C. Zeneca D. quinolones

14. **Meropenem has been initially approved for infections.**

A. respiratory B. intra-abdominal C. fungal D. gonorrhea

15. **Levaquin is the first once-a-day antibiotic proven effective against:**

A. acute maxillary sinusitis B. chronic meningitis C. N. gonorrhea

16. **There is up to 98% decreased absorption of Levaquin when given with:**

A. iron preparations B. warfarin C. theophylline D. penicillin

17. **Sparfloxacin (Zagam) is contraindicated in patients with:**

A. CHF B. tachycardia C. fungal infections D. Alzheimer's Disease

18. **Grepafloxacin should be discontinued if the patient experiences rupture of a:**

A. vein B. artery C. joint D. ligament E. tendon

19. **Trovan is the first agent ever approved for oral prophylactic use in**

A. hepatitis B. endocarditis C. lumbar punctures D. surgery

20. **is used against life-threatening VREF bacteremia.**

A. Synercid B. Probenecid C. Raxar D. Trovan E. none of these

Chapter II Pharmacology Update (Cardiovascular) Pages 35-41

21. Verapamil is used for slowing arrhythmias such as

A. V fibrillation B. atrial fibrillation C. heart block

22. **Adenosine works by slowing the initiation of the SA node**

A. conduction B. reentry C. impulses D. innervation E. rhythm

23. **when administering adenosine, you must observe the cardiac monitor for:**

A. heart block B. tachycardia C. flutter D. fibrillation E. asystole

24. **MgSo4 may be given prophylactically for the acute patient.**

A. CHF B. fibrillation C. asystole D. MI E. bradycardia

25. **Inocor is used for short-term management of in patients.**

A. CHF B. fibrillation C. asystole D. MI E. bradycardia

26. **Cilostazol relieves symptoms of intermittent claudication by inhibiting:**

A. blood coagulation B. platelet aggregation C. vasospasm

Chapter II Pharmacology Update (Respiratory) Pages 42-45

27. Zeneca is the first of a new class of agents for treating

A. heart block B. heartburn C. asthma D. cancer E. CHF

28. **Zanamivir reduced the duration of major symptoms by one to 2-1/2 days.**

A. asthma B. cold C. arthritis D. diarrhea E. influenza

Chapter II Pharmacology Update (Musculoskeletal) Pages 45-48

29. Zanaflex is the first new oral drug for muscle

A. weakness B. rigidity C. injury D. spasticity E. atrophy

30. **Celecoxib is indicated for relief of symptoms of**

A. osteoarthritis B. cancer C. muscle spasm D. hepatitis

Chapter II Pharmacoloav Update (Oncoloav) Pages 49-55

31. The PRINCIPLE of chemotherapy is to administer the tolerable drug dose.

A. minimum B. maximum C. extreme D. best E. generally

32. **These drugs have a greater ability to attack cells in the resting phase:**

A. antitumor antibiotics B. alkylating agents C. nitrosoureas

33. **M.O.P.P. stands for: , Oncovin, Procarbazine, and Prednisone.**
A. Maran B. Marinol C. Mabilone D. Marplan E. Nitrogen mustard

34. **Docetaxel is indicated for patients with metastatic cancer.**

A. bladder B. bone C. brain D. breast E. liver

35. **Ontak is the first drug specifically indicated to treat recurrent**

A. CTCL B. CMV C. breast cancer D. Hodgkin's Disease

Chapter II Pharmacology **Update (Neurological) Pages 56-65**

36. Prozac interacts with many other drugs; carbamazepine, insulin, and
A. antacids B. dilantin C. valium D. penicillin E. erythromycin

37. **Methemoglobinemia has occurred when an OTC vaginal cream was used to treat:**

A. yeast infections B. diaper rash C. sore throat D. diabetes

38. **Optimal conscious sedation/analgesia is achieved when the patient:**
A. is unresponsive B. recalls entire procedure C. retains gag reflex

39. **is recommended as a replacement for diazepam for conscious sedation.**

A. flourazepam B. morphine C. chloral hydrate D. Midazolam

40. **Managing adequately during the first procedure, usually helps reduce the anxiety associated with future procedures.**

A. pain B. sedation C. anxiety D. nausea E. the family

41. **The goal (of Narcan) is to reverse the depressant effect of opioids.**
A. pain B. neurological C. slight D. severe E. respiratory

42. **A dose of nalmefene is usually enough to reverse most opioids.**

A. large B. multiple C. small D. single E. double

43. **The person evaluating the response of the patient to the drugs, must the person performing the procedure.**

A. always be B. supervise C. not be D. instruct E. none of these

44. **The duration of the post-procedure recovery period may vary depending on the type and of sedative/analgesia administered.**

A. administration B. amount C. function D. route E. none of these

Chapter II Pharmacoloav Update (Gastrointestinal) Pages 65-70

45. Prilosec is an anti-ulcer drug that is becoming more useful in treating severe:

A. esophagitis B. duodenal ulcer C. stomach ulcer D. stomatitis

46. **Lispro may improve postprandial gylcemic control by mimicking the body's natural rapid insulin output after**
A. an injection B. sleeping C. bedtime D. fasting E. a meal

47. **Rosiglitazone increases sensitivity to insulin and decreases glucose output.**
A. stomach B. hepatic C. intestinal D. pancreatic E. pharyngeal

48. **Adverse reactions to Miglitol include: abdominal pain, diarrhea, and**
A. urticaria B. constipation C. flatulence D. hyperglycemia

49. **Orlistat works by blocking in the GI tract.**
A. fats B. proteins C. carbohydrates D. digestion E. water

50. **Aciphex is indicated for long-term treatment of disease.**
A. diarrhea B. Zollinger-Ellison C. Addison's D. gastric acid

Chapter II Pharmacology Update (Psvchotropics) Pastes 72-96

51. Remeron is particularly useful in reducing anxiety and problems which often accompany depression.
A. sexual B. sleep C. visual D. mania E. drowsiness

52. **Wellbutrin is used to treat depression and recently has been found to relieve symptoms of**
A. gastritis B. tremors C. ADHD D. Anxiety E. constipation

53. **MAOI's are usually contraindicated in asthma, CHF, and**
A. diabetes B. gastric ulcers C. alcoholism D. Addison's disease

54. **The most common side effects of Depakote are drowsiness and**
A. vomiting B. headache C. diarrhea D. anxiety E. nausea

55. **Adderall is a drug containing mixed salts of a single-entity product.**
A. magnesium B. amphetamine C. TCA D. MAOI E. benzodiazepine

56. **At least should elapse between discontinuing MAOI therapy and initiating the use of tricyclics.**
A. ten days B. 21 days C. one week D. one month E. 14 days

57. **BuSpar is often prescribed to people with anxiety disorder.**
A. pre-op B. alcohol withdrawal C. agitation D. generalized

58. **Tranxene is used as an anti-anxiety drug and for**
A. alcohol withdrawal B. pre-op anxiety C. generalized anxiety

59. **Tybatran is used as an anti-anxiety drug for tension and**
A. pre-op anxiety B. alcohol withdrawal C. agitation D. generalized anxiety

60. **Patients receiving antipsychotic drugs should have an evaluation of:**
A. thyroid tests B. liver function tests C. brain scan D. liver scan

61. **Serentil has generally side effects, with milder hypotensive effects than Thorazine.**
A. more severe B. CNS C. sedating D. fewer E. more

62. **Compazine is more often used as an antiemetic; can be used for**

A. diarrhea B. constipation C. sedation D. sleep E. antacid

63. **Pimozide works by blocking receptors and takes about two weeks to work.**

A. ACTH B. neural C. dopamine D. brain E. serotonin

64. **Risperdal is indicated for the management of disorders.**

A. psychotic B. anxiety C. neurotic D. ADHD E. dissociative

65. **Too much dopamine causes nerve impulses in the brain stem to be transmitted than normal.**
A. faster B. slower

66. **Extrapyramidal side effects, or adverse neurological effects may occur during the phase of drug therapy.**

A. involuntary B. early C. middle D. late E. voluntary

67. **This side effect (Parkinsonism) involves motor retardation or**
A. nausea B. akinesia C. dry mouth D. vomiting E. blurred vision

68. **Some symptoms of EPS include: fatigue, drowsiness, drooling, and**

A. dry mouth B. blurred vision C. mania D. weakness E. tremors

69. **Inderal, used to treat hypertension, is also used to treat migraines and:**

A. psychosis B. diabetes C. bradycardia D. Parkinson's symptoms

Chapter III Pharmacology Update (Drug Abuse/Legal Issues) Pages 97- 99

70. **Trexan is administered to the person after total from the narcotic.**

A. intoxication B. rehabilitation C. addiction D. detoxification

71. **The usual side effects of Timolol Eye Drops are: dyspepsia, hypotension, and:**

A. fatigue B. hypertension C. vomiting D. diarrhea

Chapter III Pharmacology Update (Oral Contraceptives) Pages 100-103

72. **The "mini-pill" contains only progestin, it must be taken**

A. for 21 days B. every day C. after meals D. twice daily

73. **Most combination contraceptives will begin on the first after menses.**

A. Sunday B. Monday C. day D. evening E. cycle

74. **"Plan B11 is the first dedicated pill developed in the U.S. to prevent pregnancy after unprotected intercourse.**

A. estrogen-only B. progestin-only C. mini D. abortion

Chapter III Pharmacology Update (Hepatitis Update) Pages 104

75. **The immunization (Heptavax-B) apparently has a higher rate of if given in the deltoid for some unknown reason.**

A. potency B. nausea C. side effects D. rashes E. effectiveness

Chapter III Pharmacology Update (HIV/AIDS) Pages 105-110

76. Usually **is the first drug used to treat the HIV viral infection.**

A. Retrovir B. Saquinavir C. AZT D. ddI E. ddC

77. **Coadministration of ritonavir and non-sedating may produce life-threatening situations.**

A. anti-virals B. cough syrups C. OTC drugs D. antihistamines

78. **The patient must take capsules of amprenavir per dose.**

A. two B. four C. six D. eight E. ten

79. **Amprenavir may be taken with or without food, but avoid taking it with a meal.**

A. high protein B. low carbohydrate C. low-fat D. high-fat

Chapter III Pharmacology Update (Elderly Drug Therapy) Pages 111-127

80. The main factors that affect drug therapy in the elderly are gastric emptying time, and rise in gastric juices.

A. decreased B. increased

81. **In aging, there is diminished renal blood flow,** and ,
A. reabsorption B. increased filtration C. increased secretion

82. **A condition under which the need for calcium rises; diet.**
A. low sugar B. low protein C. low phosphate D. high sodium

83. **It's easy to miss adverse drug reactions, because many reactions such as confusion, , or constipation, are common (in the elderly).**
A. falling B. alcoholism C. dizziness D. flatulence

84. **The 300 mg dose (of phenytoin) may produce such effects as sleeplessness, confusion, and nystagmus in a geriatric patient with**

A. diabetes B. hypoalbuminemia C. hyperbilirubinemia D. none of these

85. **With age, a drug or active metabolites may remain in the body longer; repeated dosing may result in significant of the drug.**

A. elimination B. accumulation C. detoxification D. deactivation

86. **In older patients, these drugs (valium, etc.) will remain in the body longer and can cause daytime sedation or in the morning.**

A. excitement B. energy C. lethargy D. hunger E. anger

87. **The following drugs require dosage adjustment for patients with diminished renal function: allopurinol (Zyloprim) and:**

A. aspirin B. Lanoxin C. valium D. tylenol

88. **Demerol is another drug that poses risks to older patients with renal impairment; toxicity is caused by an active metabolite called**

A. meperidine B. hydromorphone C. neurotoxin D. normeperidine

89. **Older adults appear to be more sensitive to adverse drug reactions.**
A. anticholinergic B. sympathomimetic C. serotonin D. hepatic

90. **A common problem your history may uncover is the use of medications.**
A. analgesic B. illegal C. multiple D. outdated E. OTC

91. **Often what determines the effect of a drug is the ratio between total body and fat.**
A. water B. blood volume C. composition D. enzymes

92. **As many as of elderly patients do not administer their medications as prescribed.**
A. 5% B. 15% C. 20% D. 30% E. 40%

93. **The primary reasons for nonadherence to drug treatment in the older patient are poor communication with and declining cognitive function.**
A. their family B. their pharmacist C. their doctor D. health professionals

Appendix A Pharmacology Update Pages 128

94. **This drug formerly used to treat gastroesophageal reflux disease will no longer be marketed in the U.S.**
A. Rezulin B. Pin-X C. Propulsid D. Doxicin E. Acetylate

95. **Because the eggs are easily transmitted, even through the , pinworms can occur in the cleanest of households.**
A. air B. bed clothes C. hair D. hands E. fingernails

Appendix B Pharmacology Update Pages 129-132

96. **Factors contributing to drug polymorphism among various ethnic groups can be loosely categorized as environmental, cultural, and**
A. biological B. genetic C. social D. historical

97. **Generally, drugs that are titrated for individual tolerance or efficacy simultaneously adjust for**
A. cultures B. race C. social factors D. effectiveness

98. **If only one drug is used, blacks respond better to diuretics than to beta blockers and**
A. antidepressants B. benzodiazepines C. ACE inhibitors D. insulin

Appendix C Pharmacology Update Pages 133

99. **has recently been shown to reduce the effectiveness of certain HIV anti-viral drugs.**
A. ephedra B. ginseng C. insulin D. St John's Wort

100. **This herb, should not be used by persons with diabetes.**
A. ginseng B. ephedra C. St John's wort D. insulin E. soy