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Basic Pharmacology: Part II – Pharmacotherapeutic Issues, Drug Regulations, and Prescription Writing

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Disclaimer: *Participants must always be aware of the hazards of using limited knowledge in integrating new techniques or procedures into their practice. Only sound evidence-based dentistry should be used in patient therapy.*

Clinicians and patients recognize the major role played by drugs in modern healthcare. Hence, it is important for practitioners to have a solid understanding of pharmacology. Participants in this course will be introduced to general pharmacological principles as they relate to the use of drugs in dental practice. Pharmacotherapeutic concepts, drug regulations, and principles of prescription writing will be reviewed.

Conflict of Interest Disclosure Statement

- The authors report no conflicts of interest associated with this course.

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Overview

Clinicians and patients recognize the major role played by drugs in modern healthcare. Hence, it is important for practitioners to have a solid understanding of pharmacology. Participants in this course will be introduced to general pharmacological principles as they relate to the use of drugs in dental practice. Pharmacotherapeutic concepts, drug regulations, and principles of prescription writing will be reviewed.

Learning Objectives

Upon completion of this course, the dental professional should be able to:

- Utilize critical thinking skills in discussing the concept of pharmacotherapy.
- Identify the content and format of labeling for human prescription drug and biological products.
- Understand basic concepts of pharmacogenomics.
- Identify and discuss "at risk" populations such as the fetus, infants, children, elderly and those with liver and kidney disease for drug-related adverse effects.
- Discuss the causes of non-adherence to recommended therapeutic strategies.
- Be familiar with the regulatory basis of manufacturing, distributing and prescribing drugs.
- Identify and discuss the essential components of a legal prescription.
- Identify, discuss, and implement the principles of good prescription writing.

Course Contents

Introduction

Historically, the clinician was responsible for information about the sources, physical and chemical properties, compounding, and dispensing of drugs. These activities are now delegated to pharmacologists and pharmacists. Today, the practitioner's responsibility requires a sound understanding of basic pharmacological principles. These principles apply to all drugs and are predicated on pharmacodynamic, pharmacokinetic, and pharmacotherapeutic variables.

Pharmacodynamics relates to the molecular interactions between body constituents and drugs. It is concerned with issues related to biochemical and physiological mechanisms of drug actions and are based on the concept of drug-receptor interactions. Pharmacodynamics describes the effect of drugs quantitatively in order to determine potency, efficacy, and toxicity. A review of pharmacodynamic principles is presented elsewhere.[1]

Pharmacokinetics relates to the mechanisms of drug absorption, distribution and redistribution,

metabolism or biotransformation, and the excretion or clearance of drugs from the body. Pharmacokinetic variable are important determinants of the dosing regimen required for a drug to reach and maintain therapeutic concentrations in the body for optimum efficacy without causing toxicity. A review of pharmacokinetic principles is presented elsewhere.[1]

Pharmacotherapeutics

Pharmacotherapy relates to the use of drugs in the prevention and treatment of disease. It is the "art and science" of applying drug-related didactic knowledge (pharmacodynamics and pharmacokinetics) and making therapeutic decisions that are the most likely to benefit a specific patient. Therefore, patient-related variables influence the design, implementation, monitoring, evaluating, and adjusting of drug therapy; and the education and motivation of patients to adhere to therapeutic recommendations.

To determine patient-related variables that will impact on the success or failure of drug therapy, clinicians must gather patient-specific information, i.e., obtain complete and accurate medical histories. From this information the clinician must develop a problem list and identify the potential for drug and/or dosage related adverse effects in "at risk" individuals such as the fetus, an infant, a child, a pregnant woman, a frail elderly, or one with liver and kidney disease; and consider factors that may affect adherence.

Drug-related Knowledge Base

The U.S. Food and Drug Administration (FDA) have specific requirements on content and format of labeling for human prescription drug and biological products.[2] The labeling (also known as the "package insert") contains scientific information needed for the safe and effective use of drugs. The labels are written for healthcare practitioners because prescription drug use requires professional supervision by a clinician licensed by law to administer such drugs.

The labeling is accurate and does not contain promotional or misleading information such as implied claims for drug use. It is updated when new information becomes available that causes the labeling to become inaccurate. Whenever possible, labeling is based on data derived from human experience. Manufacturers are required to submit to the FDA prescription drug labeling information under specific headings and subheadings, and in a specified order (Table 1).[2]

DailyMed is the official source of FDA label information (package inserts).[3] This website provides a standard, comprehensive, up-to-date, look-up and download resource of medication content and labeling found in medication package inserts. The drug labeling information on this website is the most recent submitted to the FDA, although these labels have been reformatted to make them easier to read and may include strengthened warnings undergoing FDA review.

Pharmacogenomics

The dose of a drug required to produce a specific response in an individual is the ***individual effective dose***. ***Genetic polymorphisms*** are responsible for three major types of inter-individual variations that can influence pharmacotherapy.[4,5] Genomic controls are responsible for individual differences in Phase I (i.e., oxidation and reduction) and Phase II (i.e., conjugation) reactions responsible for drug metabolism or biotransformation (i.e., ***pharmacokinetic variations***).

Genomic controls are also responsible for altered drug receptors or altered signaling pathways once a drug-receptor complex is formed (i.e., ***pharmacodynamic effects***). As well, genomic controls are responsible for ***idiosyncratic drug effects***. These are unusual, unpredictable reactions observed in a small number of individuals resulting from an interaction between a drug and some unique aspect of an individual's physiologic/ biochemical makeup.

When a drug's usual effect is produced at an unexpectedly high dose, the individual is said to be ***hyporeactive***; when the usual effect of a drug is produced at an unexpectedly low dose, the person is said to be **hyperreactive**. An individual who experiences decreased response to a drug as a result of prior exposure is said to have developed **tolerance**. Tolerance that develops rapidly, following the administration of only a few doses of a drug, is defined as ***tachyphylaxis***.

Table 1. Full content and format of labeling for human prescription drug and biological products.

Warning Box

1. Indications and Usage
2. Dosage and Administration
3. Dosage Forms and Strengths
4. Contraindications
5. Warnings and Precautions
6. Adverse Reactions
7. Drug Interactions
8. Use in Specific Populations
   - i. Pregnancy
   - ii. Lactation
   - iii. Females and males of reproductive potential
   - iv. Pediatric use
   - v. Geriatric use
9. Drug Abuse and Dependence
   - i. Controlled substance
   - ii. Abuse
   - iii. Dependence
10. Overdose
11. Description
12. Clinical Pharmacology
    - i. Mechanism of action
    - ii. Pharmacodynamics
    - iii. Pharmacokinetics
13. Nonclinical Toxicology
    - i. Carcinogenesis, mutagenesis, impairment of fertility
    - ii. Animal toxicology and/or pharmacology
14. Clinical Studies
15. References
16. How Supplied/Storage and Handling
17. Patient Counseling Information

Weight of the Patient

The optimum therapeutic dose intended to produce a specific effect in an individual is generally determined in terms of the amount of drug per kilogram of body weight of that person (1 kg = 2.2 lbs). However, it must be kept in mind that drug dosages may have to be altered in the presence of such factors as age (Figure 1), obesity, and various disease states such as liver and kidney disease that affect pharmacodynamic and pharmacokinetic processes.

In general, if the manufacturer's ***maximum recommended dose*** (MRD) of a drug for a healthy adult per day is 60 mg/kg/day to be administered in three equal doses and the patient weighs 143 lbs (i.e., 65 kg), then the daily MRD for that individual is 3900 mg (60 mg/kg/day x 65 kg) to be administered in 1300 mg doses three times a day. It is of note that if a person weighs more than 165 lbs (i.e., ≥75 kg), the MRD should only be exceeded with extreme caution.

Pregnancy

Each drug has a threshold concentration above which fetal abnormalities can occur and below which no effects are discernible. Whether a

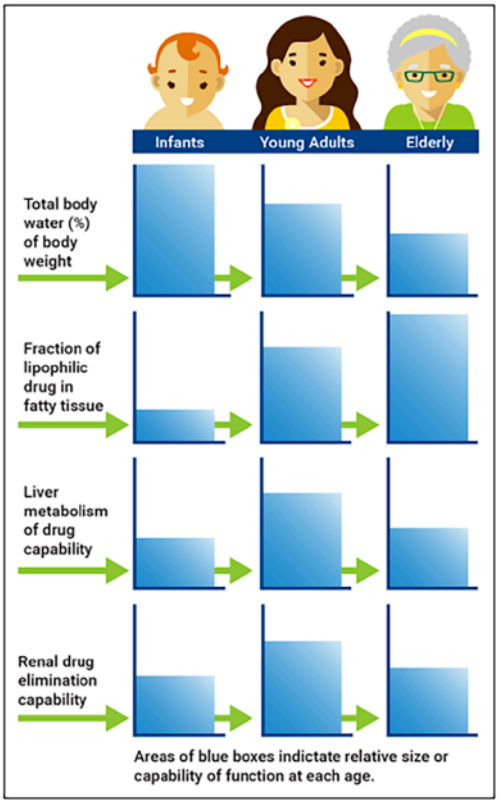

Figure 1. Age-related pharmacokinetic variables.

drug reaches the threshold concentration in the fetus depends on determinants (i.e., the drug's molecular weight, lipid solubility, pKa, and plasma protein binding) that affect a drug's ability to translocate across biological membranes and in this case that includes the placental barrier as well.

The genetic determinants of both the mother and the fetus will influence the extent to which an agent will affect the developing fetus. If threshold concentration occurs, major malformations are usually the result of fetal exposure to a drug during organogenesis (first trimester), while exposure during the second and third trimesters primarily affects organ function. However, it is paramount to recognize that human teratogenicity is not predictable.

In 2014, the FDA amended its regulations governing the content and format of labeling for human prescription drugs and biological products.[2] The amendment, which became effective on June 30, 2015, requires the removal of the old pregnancy categories A, B, C, D, and X from all drug product labeling and the inclusion of a new "Pregnancy" subsection that provides consistent information about risks to the fetus (Box A).[3]

Lactation

Factors that influence the ability of a drug to translocate across biological membranes will affect its concentration in milk. Since milk is generally more acidic (pH 6.8) than plasma (pH 7.4), milk can act as an "ion trap" for weak bases and, at equilibrium, basic drugs may become more concentrated in milk than in the maternal circulation. Conversely, acidic drugs are limited in their ability to enter milk and a net transfer of the drug from milk to plasma occurs.

The 2014 amendment to the FDA's regulations governing the content and format of labeling for human prescription drugs and biological products requires the inclusion of a "Lactation" subsection with a summary of the risks of using a drug during lactation.[2,3] If data demonstrate that the drug is not absorbed systemically by the mother, it is so stated in the risk summary. If data demonstrate that the drug is absorbed systemically, the summary includes a risk statement.

Box A. Elements of the "Pregnancy" subsection of the FDA's new labeling requirements for drugs.

- A summary of the risks of using the drug during pregnancy.
  - If data demonstrate that the drug is not absorbed systemically, the risk summary contains a specified statement regarding this fact.
  - If data demonstrate that the drug is absorbed systemically, the risk summary is based on data from all relevant sources (human, animal, and/or pharmacologic) that describe the risk of adverse developmental outcomes.
- Relevant information, if it is available, to help healthcare providers make prescribing decisions and counsel women about the use of the drug during pregnancy.
  - This includes information on disease-associated maternal and/or embryo/fetal risk, dose adjustments during pregnancy and the postpartum period, maternal adverse reactions, fetal/neonatal adverse reactions, and/or the effect of the drug on labor or delivery.
- A specific statement about the existence of a pregnancy exposure registry for the drug.
  - When such a registry exists for the drug, the telephone number and/or information needed to enroll in the registry or to obtain information about the registry is included at the beginning of the "Pregnancy" subsection.

The summary also provides, to the extent it is available, relevant information on the presence of the drug in human milk, effects of the drug on the breast-feeding child, and effects of the drug on milk production. The "Lactation" subsection also includes, to the extent it is available, relevant information concerning ways to minimize drug exposure in the breast-feeding child. In addition, the labeling includes data that are the basis for the risk summary.

Females and Males of Reproductive Potential

The 2014 amendment to the FDA's regulations governing the content and format of labeling for human prescription drugs and biological products also requires the inclusion of a "Females and Males of Reproductive Potential" subsection.[2,3] The subsection provides guidance when pregnancy testing or contraception is required or recommended before, during, or after drug therapy; or when there are human or animal data that suggest drug-associated fertility effects.

Pediatric Patients

Pediatric drug therapy presents a unique challenge to clinicians. Often there is a paucity of specific pharmacokinetic and pharmacodynamic data for the pediatric population. Dosage forms designed with the adult population in mind and the dosages cannot easily be individualized for children. Even when appropriate dosage forms for children are available palatability, resistance to taking medications and adherence issues may hinder optimal therapy.

Although there are many rules and formulae to calculate drug dosages for children, weight-based dosing recommendations by manufacturers provide the most reasonable approach.[6] Information on a specific drug prescribed to a child can be found in the "Dosage and Administration," "Contraindications," "Warning and Precautions" and "Adverse Effects" sections; and in the "Pediatric use" subsection of the drug's labeling.[3]

The maximum safe dose of a drug should be carefully calculated for each child. For example, if the MRD of lidocaine, 2% with epinephrine 1:100,000, is 3.2 mg/lb, the maximum safe dose for a child of 25 lbs in milligrams, milliliters, and cartridges would be as follows:

Step 1 – MRD in mg
MRD in mg/lb x weight of patient in lbs = Total MRD in mg
i.e., 3.2 mg/lb x 25 lbs = 80 mg

Step 2 – MRD in ml
Total MRD in mg ÷ mg per ml = Total MRD in ml
i.e., 80 mg ÷ 20 mg/ml (in a 2% formulation) = 4.0 ml

Step 3 – MRD in cartridges
Total MRD in mg ÷ mg/cartridge = Total MRD in cartridges
i.e., 80 mg ÷ 36 mg/cartridge (in a 1.8 cc cartridge) = 2.22 cartridges

Similarly, if the MRD of mepivacaine, 3% plain, is 3 mg/lb, the maximum safe dose for a child of 25 lb in milligrams, milliliters, and cartridges would be as follows:

Step 1 – MRD in mg
MRD in mg/lb x weight of patient in lbs = Total MRD in mg
i.e., 3 mg/lb x 25 lbs = 75 mg

Step 2 – MRD in ml
Total MRD in mg ÷ mg per ml = Total MRD in ml
i.e., 75 mg ÷ 30 mg/ml (in a 3% formulation) = 2.5 ml

Step 3 – MRD in cartridges
Total MRD in mg ÷ mg per cartridge = Total MRD in cartridges
i.e., 75 mg ÷ 54 (in a 1.8 cc cartridge) = 1.38 cartridges

Geriatric Patients

The use of drugs in elderly patients is another challenging area of clinical practice.[7-9] The pharmacokinetics and pharmacodynamics of drugs are altered by age-related physiologic changes. The increased incidence of multiple chronic illnesses, the disproportionately high use of prescription and over-the-counter medications, inadequate nutrition, and poor adherence also contribute to the problem and lead to more adverse drug effects among the elderly.

Therapeutic target concentrations of drugs in the elderly population are also difficult to define

because of marked inter-individual variations. Conservative dosing and close monitoring for dose-related effects is imperative. Information on a specific drug prescribed to the elderly can be found in the "Dosage and Administration," "Contraindications," "Warning and Precautions" and "Adverse Effects" sections; and in the "Geriatric use" subsection of individual drug labeling.[3]

Patients with Liver Disease

The spectrum of liver disease is wide. Most of the underlying pathophysiologic mechanisms relate to autoimmune diseases, viral infections and hepatotoxic agents leading to hepatitis, cirrhosis, hepatocellular carcinoma, and increased risk of bleeding. Liver disease is one of the most common causes of morbidity in patients receiving drugs and, in the presence of liver disease, most adverse drug reactions are related to altered pharmacokinetics.

The most widely accepted method to estimate the ability of the liver to metabolize drugs is to determine the patient's ***Child-Pugh score*** (Table 2).[10-12] The Child-Pugh score consists of five laboratory tests or clinical symptoms: total bilirubin, serum albumin, prothrombin time or International Normalized Ratio (INR), ascites, and hepatic encephalopathy. Each of these five areas is given a score from 1 (normal) to 3 (severely abnormal) and the scores are totaled.

In general, for drugs metabolized by the liver, a score of ≤ 7 requires no modification of therapy; a score of 8 to 9 is grounds for a moderate decrease (≈25%) in the daily dose; and a score of ≥ 10 indicates a need for significant decrease (≈50%) in daily dosing. Information on a specific drug prescribed to patients with liver disease can be found in the "Dosage and Administration," "Contraindications," "Warning and Precautions" and "Adverse Effects" sections of the drug's labeling.[3]

Patients with Chronic Kidney Disease

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative defines chronic kidney disease (CKD) as the presence of kidney damage or a reduction in the ***glomerular filtration rate*** (GFR) for three months or longer.[13] CKD can affect multiple organ systems and these pathophysiologic changes have been associated with profound alterations in the pharmacokinetics and pharmacodynamics of many drugs.

The gold standard to measure kidney function is the GFR. However, FDA-approved drug labels, which provide recommendations for adjustments of drug dosages for patients with impaired kidney function are, most commonly, based on the ***estimated creatinine clearance*** (eCrCl) determined by the ***Cockcroft-Gault equation***.[14] In the equation, eCrCl is expressed in mL/min, age in years, weight in kilograms, and serum creatinine (S_{cr}) in mg/dL:

$$eCrCl = (140 - age \times weight \times 0.85 \text{ (for females)}) \div S_{cr} \times 72$$

The normal range for eCrCl for men and women 40 years of age or older is 107-139 mL/min and 87-107 mL/min, respectively. After 20 years of age, eCrCl is reduced by 6.5 mL/min every 10 years. In drug dosing, the eCrCl is used as a surrogate of GFR to determine renal function (Figure 2). The eCrCl is slightly higher than true

Table 2. Child-Pugh classification for chronic liver disease.*

Tests/Symptoms	Score 1 point each	Score 2 points each	Score 3 points each
Total bilirubin in mg/dL	< 2.0	2.0-3.0	> 3.0
Serum albumin in mg/dL	> 3.5	2.8-3.5	< 2.8
Prothrombin time in seconds over control or the INR	< 4 (INR: < 1.7)	4-6 (INR: 1.7-2.3)	> 6 (INR: > 2.3)
Ascites	Absent	Slight	Moderate
Hepatic encephalopathy	None	Moderate	Severe

*A score of 5 indicates normal liver function, whereas a score of 15 indicates extreme dysfunction.

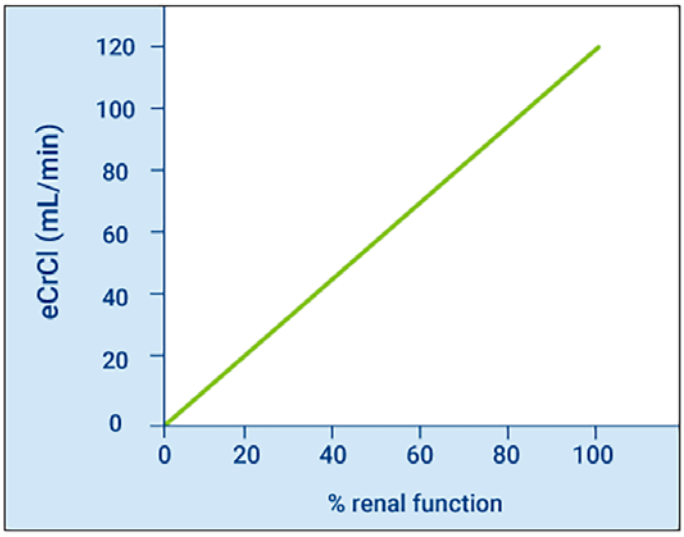

Figure 2. eCrCl, a surrogate for GFR, and estimated percent renal function.

GFR because, in addition to being filtered by the glomeruli, creatinine is also excreted by the proximal tubules.

Patients on Dialysis

Drug prescribing is further complicated when patients are put on dialysis because some drugs may be lost in the dialysis bath.[15] The extent to which a drug is removed by dialysis is dependent on the drug's molecular weight, plasma protein binding, volume of distribution, water/lipid solubility, and plasma clearance. In addition, the dialysis of drugs will depend on the technical aspects of the dialysis procedure and the type of dialysis membrane used.

In ***peritoneal dialysis***, the dialysis membrane is the naturally occurring peritoneal membrane; in ***hemodialysis*** the membrane is synthetic with fixed pore size. As a general rule, drugs with large molecular weights tend to cross the peritoneal membrane to a greater extent than the hemodialysis membrane. Since only the free drug can cross dialysis membranes, plasma protein binding is an important factor in determining the dialyzability of drugs.

However, plasma protein binding may decrease in uremic plasma increasing the dialyzability of some drugs; and the peritoneal membrane does permit the passage of some proteins leading to some drug-protein dialysis. Conversely, high lipid solubility and low protein binding contribute to a larger volume of distribution, i.e., a drug is widely distributed throughout tissues. Drugs with large volume of distribution are present in plasma in small amounts and are dialyzed minimally.

Drug dialysis data are not readily available for many drugs.[3] However, guidelines designed to provide information regarding the dialyzability of drugs is available.[15] In general, if hemodialysis and peritoneal dialysis enhances plasma clearance of a drug by more than 30%, supplemental dosing may be required or dosing after dialysis should be considered. If dialysis does not have a clinically important effect on plasma clearance supplemental dosing is usually not required.

Non-adherence

It is a generally accepted fact that many patients are not adhering to their medication regimen as prescribed.[16-19] ***Non-adherence*** can be intentional (actively choosing not to adhere) or unintentional (e.g., passively inconsistent medication-taking behavior including forgetfulness or carelessness). Determinants of non-adherence include the disease, the patient, the practitioner, the treatment regimen, economic factors, and the interaction of each of these factors.

Patient trust in the clinician and treatment as established during the office visit is important. Patients tend to be adherent if they have a good understanding of the illness and the therapy. Therefore, good communication between clinicians and patients is a major factor affecting

adherence. A positive office visit, along with individualized regimens and good follow-up on the part of the clinician, improve adherence.

When an illness is serious or disabling, the patient will likely follow the therapeutic regimen. The longer the duration of treatment, the less likely it is that the patient will adhere to the regimen over time. This is especially true if symptoms are relieved before drug therapy is to be discontinued. The regimen itself may also be discouraging or confusing because of multiple drug use, scheduling of dosages, and side effects. Finally, cost may be a major contributing factor.

In children, the major reason for non-adherence is a dislike for the taste or smell of the medication. If it is frustrating to the parent/guardian to give the medication, they are more likely to skip doses or discontinue the medication with the disappearance of symptoms. If the child is attending school, the regimen should be convenient and coordinated with the school schedule. Consider recommending specific times rather than generalize.

Common causes of non-adherence in elderly patients include failure to fill prescriptions due to transportation problems and expense. Other factors include a lack of trust or confidence in the doctor or therapy and poor comprehension of the regimen. Difficulty in opening packages or swallowing pills, poor memory, visual or hearing impairment may also contribute to non-adherence. Repetition of directions with written instructions and clear labeling are helpful.

Adverse Drug Effects

Drugs, including herbal remedies and various dietary supplements, seldom exert their beneficial effects without also causing ***adverse drug effects*** (ADEs). The inevitability of this therapeutic dilemma lends credence to the statement that there are no "absolutely" safe biologically active agents. ADEs range from mild to severe reactions and can lead to hospitalization, permanent disability, or death. ADEs may be predictable and unpredictable (Table 3).

Predictable ADEs, with the exception of drug overdose, are associated with the administration of therapeutic dosages of a drug. Predictable ADEs are usually avoidable, and they are responsible for most ADEs. Unpredictable ADEs are generally independent of the dose and they are usually unavoidable. While they are uncommon, unpredictable ADEs are often among the most serious and potentially life threatening, e.g., anaphylactic reaction.

Healthcare providers must be actively involved in monitoring for and reporting ADEs. In 1993, the FDA launched ***MEDWatch***, an initiative to educate healthcare professionals about the critical importance of being aware of, monitoring for, and reporting ADEs (Box B).[20] It is designed for voluntary reporting of problems associated with medical products. Importantly, reporting does not require proof of causality; a suspected association constitutes sufficient reason to report.

Drug Regulations

Until the nineteenth century, there were few standards or guidelines to protect the public from unsafe and ineffective drug, and unscrupulous purveyors. In those days there were many medicinal concoctions that, even if nontoxic, were not effective. Examples of early remedies include heroin for asthma and coughs, and rattlesnake oil for rheumatism. Codeine use started in the late nineteenth century and with that came the advent of addiction-related problems.

Table 3. Classification of adverse drug effects.

• Predictable
  ○ Overdose
  ○ Cytotoxic reactions
  ○ Drug-drug interactions
  ○ Drug-food interactions
  ○ Drug-disease interactions
	• Unpredictable
	  ○ Idiosyncratic reactions
	  ○ Immunologic/allergic reactions
	  ○ Pseudoallergic reactions
	  ○ Teratogenic effects
	  ○ Oncogenic effects

Box B. Mechanisms to report ADEs.

- FDA Form 3500 available at http://www.fda.gov/medwatch/report/hcp.htm
  - Complete Form 3500 online
  - Complete a downloaded a copy of Form 3500
    - Fax it to 1-800-FDA-0178
    - Mail the completed, postage-paid and addressed form to the FDA
  - Call 1-800-FDA-1088 to report by telephone

The first historical milestone in U.S. Food and Drug Laws was the publication of ***U.S. Pharmacopoeia*** (USP) in 1820.[21] The USP listed standards for drug purity and strength, and directions for synthesis. In 1975, the USP and the ***National Formulary*** (NF), published by the American Pharmaceutical Association (APhA) merged. The new publication, the ***U.S. Pharmacopoeia-National Formulary*** (USP-NF), is still published with regular updates.

To protect the public from deceitful and unsafe practices by manufacturers, in the early 1900s the U.S. Congress began to enact and enforce tougher drug laws.[21,22] The ***Biologics Control Act of 1902*** was enacted to ensure the purity and safety of serums, vaccines, and other similar products used to prevent or treat diseases in humans. Subsequently, Congress enacted the ***Food and Drug Act of 1906***, prohibiting interstate commerce in misbranded and adulterated drugs.

The ***Harrison Narcotic Act of 1914*** required prescriptions for products exceeding the allowable limit of narcotics and mandated increased record-keeping by physicians and pharmacists who dispensed such drugs. The **Federal Food, Drug, and Cosmetic Act of 1938** consolidated the Food and Drug Act of 1906 and its many amendments, extended control over cosmetics and therapeutic devices, and required that the safety of new drugs be established before marketing.

The ***Durham-Humphrey Amendment of 1951*** defined the kinds of drugs that cannot be safely used without medical supervision and prohibited their sale without a prescription by a licensed practitioner. The ***Kefauver-Harris Drug Amendments of 1962*** required manufacturers to prove that a drug was effective, that adverse effects observed after the drug was marketed be reported to the FDA, and that drug ingredients be listed by the generic name in labeling and advertising.

The ***Drug Abuse Control Amendments of 1965*** required accounting for drugs with potential for abuse, i.e., depressants, stimulants, and hallucinogens. The ***Comprehensive Drug Abuse Prevention and Control Act of 1970***, also known as the ***Controlled Substances Act (CSA) of 1970***, collected all legislations related to drugs with abuse potential into a single legislation and created a "closed" system for legitimate manufacturing, distribution, and dispensing of drugs.

Drugs under the Controlled Substances Act of 1970 were divided into five schedules (Table 4). The current list of controlled substances can be found in Section 1308 of the most recent issue of Title 21 Code of Federal Regulations (CFR).[23] Drugs are placed in their respective schedules based on whether they have a currently accepted medical use, their relative abuse potential, and the likelihood of causing dependence when abused.

Based on existing federal regulations, drugs fall into two major categories: ***non-prescription and prescription drugs***. Prescription drugs are further divided into ***legend drugs*** and ***scheduled drugs***. Legend drugs require a prescription because they are considered to be potentially harmful if not used under supervision by a licensed practitioner. Legend drugs are known as such because their labels bear the legend "Caution: Federal Law Prohibits Dispensing without a Prescription."

While scheduled drugs are also prescription drugs, their distribution and use are more tightly control by Federal and State regulations. A licensed practitioner who administers, prescribes, or

Table 4. Schedules of controlled substances.[23]

Schedule	Comments	Examples

Schedule I	• No currently accepted medical use in the U.S.
	• Lack of accepted safety for use under medical supervision
	• High potential for abuse
		• Schedule I substances
		  ○ heroin
		  ○ lysergic acid diethylamide (LSD)
		  ○ marijuana (cannabis)
		  ○ peyote
		  ○ methaqualone
		  ○ 3,4-methylenedioxymethamphetamine ("Ecstasy")

Schedule II/IIN	• High potential for abuse
	  ○ May lead to severe psychological or physical dependence
		• Schedule II narcotics
		  ○ hydromorphone (Dilaudid®)
		  ○ methadone (Dolophine®)
		  ○ meperidine (Demerol®)
		  ○ oxycodone (OxyContin®, Percocet®)
		  ○ fentanyl (Sublimaze®, Duragesic®)
		• Other Schedule II narcotics
		  ○ morphine, opium, codeine, and hydrocodone
		• Schedule IIN stimulants
		  ○ amphetamine (Dexedrine®, Adderall®)
		  ○ methamphetamine (Desoxyn®)
		  ○ methylphenidate (Ritalin®)
		• Other Schedule II substances
		  ○ amobarbital, glutethimide, and pentobarbital

Schedule III/IIIN	• Potential for abuse less than with Schedules I or II substances
	  ○ Abuse may lead to high psychological dependence
	  ○ Abuse may lead to low- to-moderate physical dependence
		• Schedule II narcotics
		  ○ Products containing not more than 90 milligrams of codeine per dosage unit (Tylenol with Codeine®)
		  ○ buprenorphine (Suboxone®)
		• Schedule IIIN non-narcotics
		  ○ benzphetamine (Didrex®)
		  ○ phendimetrazine
		  ○ ketamine
		  ○ anabolic steroids such as Depo®-Testosterone

Table 4. Continued.

Schedule	Comments	Examples
Schedule IV	• Low potential for abuse relative to Schedule III substances	• Schedule IV substances ○ alprazolam (Xanax®) ○ carisoprodol (Soma®) ○ clonazepam (Klonopin®) ○ clorazepate (Tranxene®) ○ diazepam (Valium®) ○ lorazepam (Ativan®) ○ midazolam (Versed®) ○ temazepam (Restoril®) ○ triazolam (Halcion®)
Schedule V	• Low potential for abuse relative to Schedule IV substances ○ Consist primarily of preparations containing limited quantities of certain narcotics	• Schedule V substances ○ Cough preparations containing not more than 200 milligrams of codeine per 100 milliliters or per 100 grams (Robitussin AC®, Phenergan with Codeine®), and ezogabine

dispenses controlled substances must register under ***Controlled Substances Act of 1970*** with the Drug Enforcement Administration (DEA) and obtain a DEA number, which must be included on every prescription for a controlled substance. Many States have additional requirements.

The ***Diversion Control Amendments of 1984***, part of the ***Comprehensive Crime Control Act of 1984***, authorizes the U.S. Attorney General to grant or deny an application for a DEA number based on the (1) recommendation of State licensing boards, (2) applicant's experience in dispensing or conducting research with controlled substances, and (3) applicant's conviction record related to the manufacture, distribution, or dispensing of controlled substances.[24]

Required Elements of a Legal Prescription

A prescription is a written, verbal, or electronic order (1) from a licensed practitioner, (2) to a pharmacist, (3) for a particular medication, (4) for a specific patient, (5) at a particular time. It has three components: a heading, a body, and a closing (Figure 3). These elements identify the prescriber and the patient; inform the pharmacist of the name, strength, and formulation of the drug to be dispensed; and provide instructions to the patient for self-administration of the drug.

Orders for legend, Schedule III, Schedule IV, and Schedule V drugs may be issued either orally or in writing. Orders for Schedule II drugs must be written. A practitioner may call-in a Schedule II prescription to a pharmacist, but the amount must be limited for the emergency period and the oral order must be followed up by a written order within 72 hours. Prescriptions must always be written legibly, words and numbers spaced out to avoid confusion, and all information verified.

Heading

The prescriber's name, i.e., the licensed practitioner's address, and phone number validate the prescription, provide contact information, and identify the practitioner's primary place of business. The patient's full first and last name are imperative, the middle initial may be helpful.

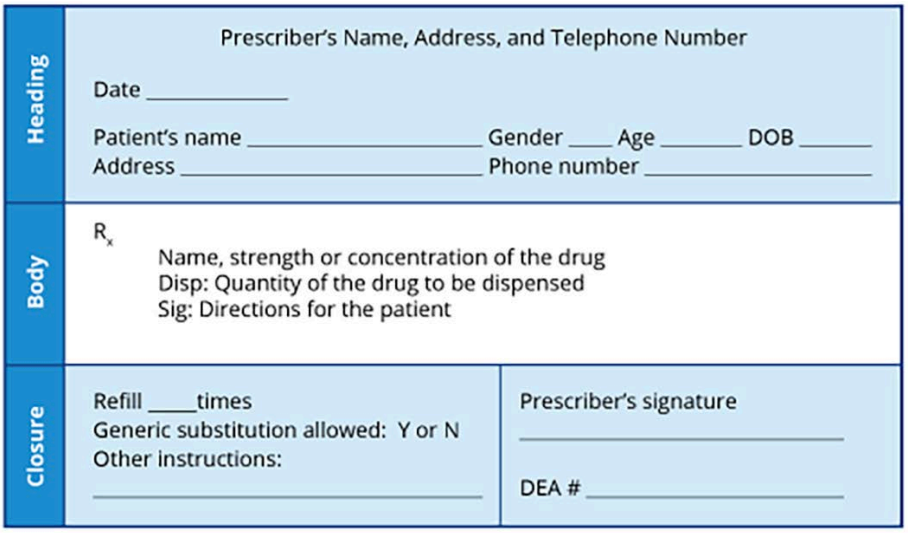

Figure3. Components of a prescription.

The patient's gender and age is useful to the pharmacist in determining the appropriateness of the medication and/or the proper dosage to be dispensed.

The date when a prescription was issued or written allows for a determination of the life of the prescription to validate refills. A prescription for legend drugs expires 1 year from the date of issue. A prescription for schedule III, IV, and V drugs expires in 6 months. A prescription for schedule II drugs expires in 7 days. These limitations placed on the life of a prescription are intended to foster ongoing patient supervision and follow-up.

Body

The body of the prescription includes the symbol RX followed by the name of the drug (generic or brand name), which must be written out in full. The strength of a drug's unit dose is to be written in the metric system, e.g., in grams (g) or milligrams (mg) for solid formulations and in milligram per milliliter (mg/ml) for liquid formulations.[25] Under directions for the patient it may be necessary to convert milliliters to a convenient household measurement (Table 5).[25]

When writing dosage strength, always use leading zeros, e.g., write 0.5 ml versus .5 ml (which can be mistaken for 5 ml); and avoid trailing zeroes, e.g., write 5 mg versus 5.0 mg (which can be mistaken for 50 mg). When the strength of a unit dose is 1 milligram or more, but less than 1 gram, it should be written in milligrams (e.g., write 200 mg, not 0.2 g). When the unit dose is 1 gram or more it should be written in grams (e.g., write 2 g, not 2000 mg).

Dispense only the necessary quantity of a drug to a patient. For example, if a patient is to take two tablets of a drug four times a day for 5 days, the total number of tablets to be dispensed would be 2 x 4 x 5 or 40 tablets. In order to discourage alterations in written prescription orders, when prescribing a controlled substance, in addition

Table 5. Common metric and household measures.[25]

Weight/abbreviation		Conversion	
kilogram	kg	1 kg	1000 g
gram	g	1 g	1000 mg
milligram	mg	1 mg	1/1000 g
pound	lb	1 kg	2.2 lb
grain	gr	1 gr	65 mg
Volume/abbreviation		**Conversion**	
liter	L	1 L	1000 ml
teaspoon	tsp	1 tsp	5 ml
tablespoon	tbsp	1 tbsp	15 ml
drop	gtt	15 gtt	1 ml
fluid ounce	fl oz	1 fl oz	30 ml

Table 6. Common Latin abbreviations that may be used in prescription writing.[25]

Abbreviation	From the Latin	Meaning
a.c.	ante cibum	before meals
admov.	admove	apply
alt. h.	alternis horis	every other hour
a.m.	ante meridiem	morning, after noon
bis	bis	twice
b.i.d.	bis in die	twice daily
cap., caps.	capsula	capsule
cc	cum cibos	with food
e.m.p.	ex modo prescripto	as directed
h.s.	hora somni	at bed time
notc.	nocte	at night
p.c.	post cibum	after meals
p.m.	post meridiem	evening or afternoon
prn	pro re nata	as needed
p.o.	per os	by mouth
q.a.d.	quaque alternis die	every other day
q.a.m.	quaque die ante meridiem	every day before noon
q.h.	quaque hora	every hour
q.h.s.	quaque hora somni	every night at bedtime
q.1h	quaque 1 hora	every 1 hour
q.d.	quaque die	every day
q.i.d.	quarter in die	four time a day
qqh	quarter quaque hora	every four hours
stat	statim	immediately
syr	syrupus	syrup
tab	tabella	tablet
t.i.d.	ter in die	three times daily
u.d., ut. dict.	ut dictum	as directed

to writing the number of tablets or capsules to be dispensed, the amount must also be written-out longhand, e.g., Disp #20 (twenty).

Latin and other abbreviations (Table 6) are authorized in prescription writing.[25] They save time and make alteration of a prescription by the patient more difficult. ***However, abbreviations are more likely to be misinterpreted and lead to potentially serious mistakes. Practitioners should avoid using abbreviations and write-out instructions in full.*** For example, an instruction for the patient should be written-out as follows: "Take two tablets four times a day for 5 days."

Closing

The closing must exhibit the prescriber's signature and DEA # (if applicable). It may also contain additional instructions to the pharmacist, e.g., whether generic substitution is allowed and/or to include warnings on container labels such as "May cause drowsiness," "Take with food," or "Do not take with grapefruit juice." A pharmacist cannot refill a prescription without authorization, to avoid interrupting maintenance therapy, the prescriber may authorize refills on a written prescription.

Refills authorized on an order for a legend drug are valid for 1 year after the date of issue. For example, it is common practice to prescribe legend drugs for the treatment of a chronic condition such as hypertension to last for 90 days and to authorize three refills. An order for Schedule III, Schedule IV, and Schedule V drugs may be refilled up to five times within six months after the date of issue. Refilling orders for Schedule II drugs is prohibited, they require new prescriptions.

Principles of Good Prescribing

Prescribing medications is one of the main strategies to the prevention and treatment of disease in modern healthcare. Per capita utilization of prescription drugs, predicated on the top 200 drugs dispensed by U.S. community pharmacies, is about 12 prescriptions per person per year.[26-28] Adults over 50 years of age consume the largest number of prescription medications and account for 64% of the total number of prescriptions dispensed.

While drugs have the capacity to enhance health, they all have the potential to cause harm if prescribed inappropriately. For this reasons it is recommended that healthcare professionals who prescribe medications exercise critical thinking skills to ensure the safe and effective use of therapeutic agents. The following ten steps, along with ongoing self-directed learning, reflect an efficient and practical approach to prescription writing and avoiding errors (Box C).[29,30]

Summary

Successful pharmacotherapy is predicated on the application of pharmacodynamic and pharmacokinetic principles in light of knowledge gained in clinical medicine. It requires critical

Box C. Principles of good prescribing.[29,30]

1. **Be clear about the reasons for prescribing**
   - Establish an accurate diagnosis whenever possible (although this may at times be difficult)
   - Specify a clear therapeutic objective
2. **Consider the patient's drug history before prescribing**
   - Obtain an accurate list of current and recent medications (including over-the-counter and alternative medicines) and a history of prior adverse drug reactions and drug allergies
3. **Identify other factors that might alter the benefits and risks of treatment**
   - Consider individual risk factors that might influence the prescription (e.g., physiological changes with age and pregnancy, or impaired kidney or liver function)

Box C. Continued.

4. **Take into consideration the patient's expectations**
   - Seek to form a partnership with the patients when selecting treatments, making sure that they understand and agree with the reasons for taking the medication

5. **Select efficacious, safe, and cost-effective drugs appropriate for the patient**
   - The likely beneficial effects of a drug should outweigh any potential harms and, whenever possible, this decision should be based on published evidence
   - Choose the best formulation, dose, frequency, route of administration, and duration of treatment

6. **Adhere to guidelines**
   - Be aware of evidence-based recommendations developed by respected professional organizations
   - Balance specific drug selection considering the needs of the patient and cost
   - Identify, access, and use reliable and validated sources of information

7. **Write unambiguous legal prescriptions using the correct documentation**
   - Be aware of common factors that cause medication errors and know how to avoid them

8. **Monitor the beneficial and adverse effects of therapeutic agents**
   - Understand how to alter the therapeutic regimen as a result of this information
   - Know how to report adverse drug reactions

9. **Communicate the reasons for and document prescribing decisions**
   - Communicate clearly with the patient as well as the pharmacist
   - Give patients information about how to take the medicine, what benefits might arise, adverse effects (especially those that will require urgent attention), and any monitoring that is required
   - Document prescribing decisions in the health record accurately

10. **Prescribe within limitations of knowledge, skills and experience**
    - Always keep relevant knowledge and skills up to date
    - Be prepared to seek the advice and support of qualified professional colleagues
    - Verify all information on prescriptions

thinking skills forged during long hours of clinical practice and a life-long commitment to the disciplined study of drug- and patient-related variables. Fostered by a sincere desire to maximize therapeutic benefits, clinicians should prescribe drugs with great care.

Course Test Preview

1. All of the following statements are correct with respect to pharmacodynamics EXCEPT which one? Pharmacodynamics _____.

a. relates to the molecular interactions between body constituents and drugs
b. is concerned with issues related to biochemical and physiological mechanisms of drug actions and are based on the concept of drug-receptor interactions
c. relates to determinant of the dosing regimen required for a drug to reach and maintain therapeutic concentrations in the body for optimum efficacy without causing toxicity
d. describes the effect of drugs quantitatively in order to determine potency, efficacy, and toxicity

2. Pharmacotherapy _____.

a. is the "art and science" of applying drug-related didactic knowledge and making therapeutic decisions that are the most likely to benefit a specific patient
b. deals with the design, implementation, monitoring, evaluating and adjusting drug therapy; and educating/motivating patients to adhere to therapeutic recommendations
c. requires the gathering of patient-specific information, i.e., obtaining a complete and accurate medical history
d. All of the above are correct.

3. All of the following statements are correct with respect to FDA requirements on content and format of labeling for human prescription drug and biological products EXCEPT which one?

a. The labeling (also known as the "package insert") contains scientific information needed for the safe and effective use of drugs.
b. The labels are written for consumers, i.e., for the patients, and are intended to educate and motivate them to adhere to therapeutic recommendations.
c. Manufacturers are required to submit to the FDA prescription drug labeling information under specific headings and subheadings in a specified order.
d. Labeling is updated when new information becomes available that causes the labeling to become inaccurate.

4. Which of the following statements is correct with respect to DailyMed?

a. DailyMed is the official provider of FDA label information (package inserts).
b. The DailyMed Web site provides a standard, comprehensive, up-to-date, look-up and download resource of medication content and labeling found in medication package inserts.
c. The drug labeling information on the DailyMed Web site is the most recent submitted to the FDA, although these labels have been reformatted to make them easier to read and may include strengthened warnings undergoing FDA review.
d. All of the above are correct.

5. An unusual, unpredictable reaction observed in a small number of individuals resulting from an interaction between a drug and some unique aspect of the patient's physiologic/biochemical makeup is a genetic polymorphism-related _____.

a. idiosyncratic effect
b. alteration of pharmacokinetic variables
c. alteration of pharmacodynamic variables
d. All of the above are correct.

6. Which of the following statements is correct with respect to the weight of a patient and drug dosing?

a. The optimum therapeutic dose intended to produce a specific effect in an individual is generally determined in terms of the amount of drug per kilogram of body weight.
b. Drug dosages may have to be altered in the presence of such factors as age and various disease states such as liver and kidney disease.
c. If a patient weighs more than 165 lb. (i.e., ≥75 kg), the MRD should be exceeded with extreme caution.
d. All of the above are correct.

7. Which of the following statements is correct with respect to the 2014 amendment to the FDA's regulations governing the content and format of labeling for human prescription drugs and biological products? The amendment requires the _____.

a. removal of the old pregnancy categories A, B, C, D, and X from all drug product labeling and the inclusion of a new "Pregnancy" subsection that provides consistent information about risks to the fetus
b. inclusion of a "Lactation" subsection with a summary of the risks of using a drug during lactation
c. inclusion of a "Females and Males of Reproductive Potential" subsection, which provides guidance when data suggest drug-associated fertility effects
d. All of the above are correct.

8. Information on a specific drug prescribed to a child or a geriatric patient can be found in the drug's labeling _____.

a. "Dosage and Administration" section
b. "Contraindications," "Warning and Precautions" and "Adverse Effects" sections
c. "Pediatric use" or "Geriatric use" subsection
d. All of the above are correct.

9. Which of the following statements is correct with respect to dosage modification for drugs metabolized primarily by the liver? In general, a Child-Pugh score of _____.

a. ≤7 requires no modification of drug therapy
b. 8 to 9 is grounds for a moderate decrease (≈25%) in the daily dose
c. ≥10 indicates a need for significant decrease (≈50%) in daily dosing
d. All of the above are correct.

10. All of the following statements are correct with respect to dosing recommendations for patients with chronic kidney disease or renal failure EXCEPT which one?

a. The gold standard to measure kidney function is the estimated creatinine clearance (eCrCl).
b. FDA-approved drug labels, which provide recommendations for adjustments of drug dosages for patients with impaired kidney function, are most commonly based on the eCrCl determined by the Cockcroft-Gault equation.
c. The extent to which a drug is removed by dialysis is dependent on the drug's molecular weight, plasma protein binding, volume of distribution, water/lipid solubility, and plasma clearance; and technical aspects of the dialysis procedure.
d. In general, if hemodialysis and peritoneal dialysis enhances plasma clearance of a drug by more than 30%, supplemental dosing may be required or dosing after dialysis should be considered.

11. All of the following statements are correct with respect to adherence/non-adherence of patients to their medication regimen as prescribed EXCEPT which one?

a. Determinants of non-adherence include the disease, the patient, the practitioner, the treatment regimen, and economic factors.
b. Non-adherence is invariably unintentional (e.g., passively inconsistent medication-taking behavior including forgetfulness or carelessness).
c. In children the major reason for non-adherence is a dislike for the taste or smell of the medication.
d. Difficulty in opening packages or swallowing pills, poor memory, visual or hearing impairment contribute to non-adherence by elderly patients.

12. All of the following statements related to adverse effects associated with drugs and other medical products are correct EXCEPT which one?

a. Healthcare providers must be actively involved in monitoring for and reporting ADEs.
b. The FDA launched MEDWatch, an initiative to educate healthcare professionals about the critical importance of being aware of, monitoring for, and reporting ADEs.
c. MEDWatch is designed for compulsory reporting of problems associated with medical products.
d. Reporting problems associated with medical products does not require proof of causality; a suspected association constitutes sufficient reason to report.

13. Which of the federal regulations collected all legislations related to drugs with abuse potential into a single legislation; created a "closed" system for legitimate manufacturing, distribution, and dispensing of drugs; and created the five schedules of controlled substances?

a. *Harrison Narcotic Act of 1914*.
b. *Drug Abuse Control Amendments of 1965*.
c. *Comprehensive Drug Abuse Prevention and Control Act of 1970*, also known as the *Controlled Substances Act (CSA) of 1970*.
d. *Diversion Control Amendments of 1984*, part of the *Comprehensive Crime Control Act of 1984*.

14. Based on existing federal regulations, drugs fall into two major categories: non-prescription and prescription drugs - prescription drugs are further divided into legend drugs and scheduled drugs.

a. Ture
b. False

15. Which of the following statements is correct with respect to prescription writing?

a. A prescription is a written, verbal, or electronic order (1) from a licensed practitioner, (2) to a pharmacist, (3) for a particular medication, (4) for a specific patient, (5) at a particular time.
b. Orders for legend, Schedule III, Schedule IV, and Schedule V drugs may be issued either orally or in writing; for Schedule II drugs they must be written.
c. A practitioner may call-in a Schedule II prescription to a pharmacist, but the amount must be limited for the emergency period and the oral order must be followed up by a written order within 72 hours.
d. All of the above are correct.

16. Which of the following statements is correct with respect to the heading of a prescription?

a. The prescriber's name, address, and phone number validate the prescription, provide contact information, and identify the practitioner's primary place of business.
b. The patient's full first and last name are imperative, the middle initial may be helpful; gender and age is useful to the pharmacist in determining the appropriateness of the medication and/or the proper dosage to be dispensed.
c. The date when a prescription was issued or written allows for a determination of the life of the prescription to validate refills.
d. All of the above are correct.

17. Which of the following statements is correct with respect to the body of the prescription?

a. The body of the prescription includes the symbol RX followed by the name of the drug (generic or brand name), which must be written out in full.
b. The strength of a drug's unit dose is to be written in the metric system, e.g., in grams (g) or milligrams (mg) for solid formulations and in milligram per milliliter (mg/ml) for liquid formulations.
c. Under directions for the patient it may be necessary to convert milliliters to a convenient household measurement.
d. All of the above are correct.

18. All of the following statements are correct with respect to the body of a prescription EXCEPT which one?

a. When writing dosage strength always use leading zeros, e.g., write 0.8 ml versus .8 ml (which can be mistaken for 8 ml); and avoid trailing zeroes, e.g., write 5 mg versus 5.0 mg (which can be mistaken for 50 mg).
b. When writing dosage strength and the strength of a unit dose is 1 milligram or more, but less than 1 gram, it should be written in milligrams (e.g., write 200 mg, not 0.2 g); when the unit dose is 1 gram or more it should be written in grams (e.g., write 2 g, not 2000 mg).
c. In order to discourage alterations in written prescription orders, when prescribing a controlled substance, in addition to writing the number of tablets or capsules to be dispensed, the amount must also be written-out longhand, e.g., Disp #20 (twenty).
d. The use of abbreviations is highly encouraged because they save time and make alteration of a prescription by the patient more difficult.

19. All of the following statements are correct with respect to the closing of a prescription EXCEPT which one?

a. The closing must exhibit not only the prescriber's signature, but it must include his/her and DEA # on all prescriptions for legend and controlled substances.
b. The closing may also contain additional instructions to the pharmacist, e.g., whether generic substitution is allowed and/or to include warnings on container labels such as "May cause drowsiness," "Take with food" or "Do not take with grapefruit juice."
c. A pharmacist cannot refill a prescription without authorization, to avoid interrupting maintenance therapy; in the closing the prescriber may authorize refills on a written prescription.
d. An order for Schedule III, drugs may be refilled up to five times within six months after the date of issue; refilling an order for a Schedule II drug is prohibited.

20. Following the ten steps to good prescribing, along with ongoing self-directed learning, reflects an efficient and practical approach to prescription writing and avoiding errors.

a. True
b. False

References

1. Segelnick SL, Weinberg MA. Basic Pharmacology: Part I – Pharmacodynamic and Pharmacokinetic Principles. dentalcare.com. Accessed April 11, 2016.
2. FDA. Code of Federal Regulations (CFR) Title 21, Part 201, Labeling. Revised April 1, 2015. Accessed April 11, 2016.
3. NIH. U.S. National Library of Medicine. DailyMed. Accessed April 11, 2016.
4. Wang L, Weinshilboum RM. Pharmacogenomics - Principles of pharmacology: The pathophysiologic basis if drug therapy, 2nd ed. David E Golan (Ed). Baltimore, MD. Lippincott Williams & Wilkins. 2005. 909-916.
5. Ma Q, Lu AY. Pharmacogenetics, pharmacogenomics, and individualized medicine. Pharmacol Rev. 2011 Jun;63(2):437-59. doi: 10.1124/pr.110.003533. Epub 2011 Mar 24.
6. Cella M, Knibbe C, Danhof M, et al. What is the right dose for children? Br J Clin Pharmacol. 2010 Oct;70(4):597-603. doi: 10.1111/j.1365-2125.2009.03591.x.
7. Hughes SG. Prescribing for the elderly patient: why do we need to exercise caution? Br J Clin Pharmacol. 1998 Dec;46(6):531-3.
8. Hilmer SN, Shenfield GM, Le Couteur DG. Clinical implications of changes in hepatic drug metabolism in older people. Ther Clin Risk Manag. 2005 Jun;1(2):151-6.
9. Jansen PAF, Brouwers JRBJ. Clinical Pharmacology in Old Persons. Scientifica. 2012; Article ID 723678. doi:10.6064/2012/723678. Accessed April 11, 2016.
10. Pugh RN, Murray-Lyon IM, et al. Transection of the oseophagus for bleeding oesophageal varices. Br J Surg. 1973 Aug;60(8):646-9.
11. Cholongitas E, Papatheodorodos GV, Vangeli M, et al. Systematic review: The model for end-stage liver disease – should it replace Child-Pugh's classification for assessing prognosis in cirrhosis. Aliment Pharmacol Ther. 2005 Dec;22(11-12):1079-89.
12. Boursier J, Cesbron E, Tropet AL, et al. Comparison and improvement of MELD and Child-Pugh score accuracies for the prediction of 6-month mortality in cirrhotic patients. J Clin Gastroenterol. 2009 Jul;43(6):580-5. doi: 10.1097/MCG.0b013e3181889468.
13. Munar MY, Singh H. Drug dosing adjustments in patients with chronic kidney disease. Am Fam Physician. 2007 May 15;75(10):1487-96.
14. NIH. CKD and Drug Dosing: Information for Providers. Estimation of Kidney Function for Prescription Medication Dosage in Adults. Revised April 2015. Accessed on April 11, 2016.
15. Bailie GR, Mason NA. 2013 Dialysis of Drugs. Accessed on April 11,2016.
16. Mukhtar O, Weinman J, Jackson SH. Intentional non-adherence to medications by older adults. Drugs Aging. 2014 Mar;31(3):149-57. doi: 10.1007/s40266-014-0153-9.
17. Gadkari AS, McHorney CA. Unintentional non-adherence to chronic prescription medications: How unintentional is it really? BMC Health Serv Res. 2012 Jun 14;12:98. doi: 10.1186/1472-6963-12-98.
18. Clark N, Jones P, Keller S, et al. Patient factors and compliance with asthma therapy. Respir Med. 1999 Dec;93(12):856-62.
19. Gellad WF, Grenard JL, Marcum ZA. A systematic review of barriers to medication adherence in the elderly: looking beyond cost and regimen complexity. Am J Geriatr Pharmacother. 2011 Feb;9(1): 11-23. doi: 10.1016/j.amjopharm.2011.02.004.
20. FDA. MEDWatch: The FDA Safety Information and Adverse Event Reporting Program. Reporting By Health Professionals. Accessed April 11, 2016.
21. FDA. Significant Dates in U.S. Food and Drug Law History. Accessed April 11, 2016.
22. FDA. History of Federal Regulation: 1902–Present. Accessed April 11, 2016.
23. U.S. Department of Justice. Drug Enforcement Administration. Office of Diversion Control. Controlled Substance Schedules. Accessed April 11, 2016.
24. U.S. Department of Justice. Drug Enforcement Administration. Office of Diversion Control. Diversion Control Amendments of 1984. Title 21 Code of Federal Regulations, Part 1300-end. Accessed April 11, 2016.
25. Every Patient's Advocate. Master list of medical abbreviations. Accessed April 11, 2016.
26. Bartholow M. Top 200 drugs of 2011. Pharmacy Times. Accessed April 11, 2016.

27. Bartholow M. Top 200 drugs of 2012. Pharmacy Times. Accessed April 11, 2016.
28. Symphony Health Solutions. Top 200 Drugs of 2014: Ranked by Total Prescription Count (TRx Count). Accessed April 11, 2016.
29. Pollock M, Bazaldua OV, Dobbie AE. Appropriate prescribing of medications: an eight-step approach. Am Fam Physician. 2007 Jan 15;75(2):231-6.
30. British Pharmacological Society. Ten Principles of Good Prescribing. Accessed April 11, 2016.

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