

## BASICS IN PHARMACOLOGY and MEDICATION ADMINISTRATION

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### Key Concepts:

**Loading or priming dose:** initial dosing used to rapidly reach a therapeutic drug response

**Maintenance dose:** dosing used to maintain therapeutic response

**Enteric coating:** coating which provides relative resistance to digestive action

- Prevent decomposition of chemically sensitive drugs by gastric secretion (eg PCN G)
- To prevent dilution of drug before it reaches intestine
- To prevent nausea and vomiting induced by drug's effect stomach
- To provide delayed action of drug

### First Pass Effect:

Drugs absorbed via stomach first pass through liver (portal circulation) where they are acted upon before they enter systemic circulation

Hepatic action may be metabolize (most common) therefore decreasing dosing, activate (prodrug effect) or have no effect

Oral dosing must account for first pass effect and accordingly may be very different from IV or other parenteral dosing

**Plasma protein binding** - many drugs attach to proteins on entry into circulation

Main protein of attachment is albumin

Reversible drug-protein complex: Free drug + Protein = Drug-protein complex

Anything which alters equilibrium can alter free drug - potential for toxicity

- Low albumin (elderly, cachexia)
- Drug interaction: competition for binding site -> drug toxicities

Drug-albumin molecule too large to diffuse through blood vessel

- Bound drug is pharmacologically inactive - trapped in blood stream
- Complex becomes circulating reservoir or storage depot

Plasma protein binding is expressed as a percentage

Very high: > 90%, high: 65%-90%

Moderate 35%-65%, low 10%-34%; very low < 10%

Competition for binding sites

Displacement may cause toxicity

Example: ASA may displace protein-bound warfarin (Coumadin) -> toxicity

Hemorrhage may result (warfarin normally highly protein bound)

Hypoalbuminemia - low levels of albumin

Failure of liver to produce enough plasma protein to bind drugs

More free drug results in more free drug available

Drug dosing must be decreased to avoid toxicity with normal dose

## Tissue binding

- Fat tissue binding** - lipid soluble drugs have high affinity for adipose tissue  
Drug stored in adipose tissue - > stable reservoir due to its low blood flow  
Example: thiopental (Pentothal) may remain in fat hours after administration  
Example: marijuana can be detected up to 30 days after ingestion
- Bone tissue binding** - certain drugs have unusual affinity for bone  
Absorbed in bone-crystal surface  
Example: tetracycline can accumulate in fetal skeletal tissue -> brown teeth  
Contraindicated for prenatal or pediatric administration

## Barriers to drug distribution

- Blood-brain barrier** - special anatomic arrangement facilitates lipid-soluble drugs
- Allows distribution of only lipid-soluble drugs into brain and CSF
  - Capillary endothelial cells covered by fatty sheath of glial cells
  - Prevents entry of strongly ionized, non-lipid soluble compounds
  - Example: antibiotics must cross barrier if used to TX CNS infections  
Many do not and cannot be used to treat e.g. meningitis  
Intrathecal route circumvents barrier
- Placental barrier** - membrane layers which separate vessels of mother and fetus
- Tissue enzymes in placenta can metabolize some agents (catecholamines)
  - Does not afford complete protection to fetus
  - Non-selective passage across placenta to fetus
  - Lipid-soluble substances preferentially diffuse across
  - Also permeable to many lipid-insoluble drugs
  - Therapeutic agents may harm fetus
  - Examples: antibiotics, steroids, narcotics, anesthesia

## Half-life of a drug ( $t_{1/2}$ )

- Time required to reduce unchanged drug in body by one half at equilibrium
- Duration of a dose can be demonstrated by its biologic half-life
- Half-life varies with drug
- Shorter half-life (2-3h) requires more frequent administration than long one ( $t_{1/2} = 12$ )
- Half-life does not change with drug dose: always takes same time to eliminate  $\frac{1}{2}$  drug
- Example: 10,000 units drug with half life 4 hours is administered
  - 5000 units excreted in 4 hours (4 hours from administration)
  - 2500 units excreted in next 4 hour period (8 hrs from administration)
  - 1250 units excreted in 3<sup>rd</sup> 4 hour period (12 hrs from administration)
- Renal or hepatic dysfunction may prolong drug half-life in a given patient  
Drug dosing needs to be reduced

## Routes of Administration

ENTERAL ROUTE - most common; safest, most convenient and cost effective

### Oral absorption - Buccal and sublingual routes

**Sublingual** - drug placed under tongue to dissolve in salivary secretions e.g. NTG

- Drug (if suitable) diffuses through lipid mucus membrane
- Enters circulation direction - bypasses first pass effect;
- No gastric destruction
- Absorption is rapid - effects may become apparent within 2 minutes
- Client to refrain from swallowing as long as possible

- Example: nitroglycerine (NTG) for angina

**Buccal** administration: tablet placed between teeth and mucus membrane of cheek

- Rapid onset of action
- No first pass effect; no gastric destruction

- Example: Nicorette gum (also chewing tobacco)

### Gastric absorption

- Not important absorption site
- Length of time drug in stomach is variable determining absorption
  - Drug pH
  - Gastric motility
  - Prolongation of gastric emptying can destroy unstable drugs  
Acetaminophen (Tylenol)
- Stomach pH is low (1.4)
  - Slightly acidic drugs rapidly absorbed (e.g. barbiturates)
  - Slightly basic drugs poorly absorbed (e.g. morphine, quinine)
- Large majority of drugs are weakly basic - absorbed in small intestine  
Small intestine has alkaline pH
- Many drugs are administered on empty stomach
  - Food in stomach often decreases absorption
  - Administered on empty stomach with full glass water
- Drugs causing gastric irritation administered with food

### Small intestine absorption

- Many villi; larger absorption area than stomach
- Highly vascularized
- Poorly soluble drugs pass to and absorbed in upper portion small intestine
- Intestinal pH is alkaline (7 to 8) - absorbs nonionized basic drugs
- Increased or decreased motility may affect rate of absorption

## Rectal absorption

- Rectum has small surface area but highly vascularized -> absorption
- Avoids first pass effect: blood perfusing this region bypasses the liver
- Absorption can be erratic
  - Variability of rectal contents
  - Local drug irritation with some medication
  - Uncertainty of drug retention

PARENTERAL ROUTE - refers to administration by injection - most rapid form therapy

**Subcutaneous** - (SC) drug injected beneath skin into connective tissue or fat beneath dermis

- Drugs must be not irritating to tissue (otherwise pain, necrosis, sloughing)
- Rate may be slow - can provide sustained effect

**Intramuscular** (IM) - drug injected into skeletal muscle

- Absorption more rapid than subcutaneous due to greater vascularity

**Intravenous** - (IV) produces immediate pharmacologic response

- Drug injected into bloodstream
- Circumventing the absorption process
- IV injection should be slow

**Intrathecal** - drug injected direction into spinal subarachnoid space

- Bypasses blood-brain barrier
- Used for drugs which cannot otherwise effectively enter CSF
- Used where rapid effect desired e.g. spinal anesthesia
- Used to TX acute CNS infection

**Epidural** - injected via small catheter into epidural space

- Space outside dura mater of spinal column
- Example: opioids for pain management

**Intraarticular injection:** injected into joint cavity

Indications: pain relief, reduce inflammation, maintain mobility

Example: synovial cavity, shoulder bursae

**Intraosseous injection** - injects into bone marrow

**Intraperitoneal injection:** drugs injected in peritoneal cavity

Example: drugs used in peritoneal dialysis

**Intrapleural injection** - Drugs injected into pleural space

Example: antineoplastic drugs

## OTHER ROUTES OF DRUG ADMINISTRATION

**Pulmonary route** - drugs administered via inhalation

Drugs must be in form of fine mists (aerosols)

Provides for ready entry into bloodstream

Large surface area of lungs

Rich capillary-alveolar network

Example:

Inhalers for asthmatics: inhaled bronchodilators, inhaled steroids

Drugs administered via nebulizer - albuterol (Proventil), pentamidine

**Topical route** - skin and mucous membranes

Absorption is generally rapid

**Skin:** ointments, creams, solutions, transdermal patches

- Only lipid-soluble substances are absorbed (skin acts as lipid barrier)
- Administer only to intact skin(avoids systemic absorption of toxins)
- Massaging enhances absorption (increased capillary dilation)

**Transdermal route** - disk or patch - contains day to week supply of medication

- Absorbed at steady rate; can cause skin irritation
- Examples: nitroglycerine, hormone replacement therapy, contraceptive

**Eyes** - administered to conjunctiva or anterior chamber - local effect

- Examples: steroids, antibiotics, antiinflammatory, antihistamines

**Ears** - administered into auditory canal

- Examples: antibiotics (local infections), antiinflammatory agents, ceruminolytic

**Nasal mucosa** - administered in droplet form or specific-dose swab

- Intranasal application for systemic absorption
- Intranasal application for shrinkage of mucosa - enhance breathing

## Drug-Response Relationship

**Onset of action or latent period**

Interval between time drug is administered and first sign of effect

**Termination of action:** point at which drug effect is no longer demonstrated

**Duration of action:** period from onset of action to time when response no longer perceptible

**Minimal effective concentration:** lowest plasma level which produces desired drug effect

**Peak plasma level:** highest plasma concentration achieved from a dose

**Toxic level:** plasma concentration at which drug produces serious adverse effects

**Therapeutic range**

Range of plasma concentration which produce desired effect without toxicity

**Therapeutic index:** relationship between effective dose and toxic dose

Narrow index: therapeutic dose and toxic dosing are similar e.g. digoxin

Wide index: dose can be markedly increased without toxicity e.g. penicillin

$$TI = LD_{50}/ED_{50}$$

LD = dose with is toxic for 50% animals tested

ED = dose required to produce therapeutic effect in 50% similar population

Closer the index is to 1 -> greater danger in administering to humans

Dose which side effect or toxicity is more important than TI

Prescribers wish to avoid fatalities associated with prescribing drugs

## Drug-Receptor Terminology

**Affinity:** propensity of drug to bind or attach self to given receptor site

Example: methadone and heroin have strong affinity for the mu receptor; by contrast codeine while still effectively binding the receptor has somewhat less of an affinity.

**Antagonist:**

- Drug that combines with receptors and initiates an effect
- Posses both affinity and efficacy
- Example: morphine is an agonist to mu receptor -> pain relief

**Antagonist**

- Agent which inhibits or counteract the effects produced by other drugs
- Inhibits undesired physiologic or pathologic effects
  
- Example: antihistamine (blocks histamine release e.g in response to bee sting)  
Diphenhydramine (Benadryl) used for bee sting  
Loratadine (Claritin) used for seasonal allergies (hay fever)
- Example: H2 blockers (blocks stomach acid e.g. ranitidine (Zantac) in GERD)

**Competitive antagonist**

- Agent with affinity for same receptor site as an agonist
- Competition with agonist inhibits its action
- Increasing concentration of agonist tends to overcome inhibition
- Competitive inhibition is usually reversible
  
- Example: flumazenil (Mazicon) competes with receptors for benzodiazepines hence acts as antidote for e.g. diazepam (Valium) overdose
- Example naloxone (Narcan) used to treat opioid overdoses e.g. heroin overdose

ICU patient with heroin overdose may be alert and oriented after naloxone (Narcan) injection however naloxone has shorter half-life than heroin so if patient leaves AMA (against medical advise) he/she risks return of heroin overdose symptoms (including death) when naloxone wears off (and heroin is still active in body)

**Efficacy** (intrinsic activity)

- Ability of drug to initiate biologic activity via binding with receptor site

Example: morphine strongly binds mu receptor thus is potent pain reliever

Note: do not confuse efficacy with potency. Potency indicates what dosing is needed of a given drug to produce an effect; efficacy speaks to the ability of the drug to produce a desired response.

Example enalapril (Vasotec) is more potent (typical dose 2.5 - 5 mg) than fosinopril (Monopril) where typical dose is 20-40 mg but not necessary more effective to treat hypertension

**Noncompetitive antagonist**

- Agent that combines with different parts of receptor mechanism
- Inactivates receptor such that agonist cannot be effective regardless of concentration
- Irreversible or nearly reversible
- Much less common in clinical practice (more difficult to find clinical examples)

Example: Phencyclidine or phencyclidine (PCP) - “angel dust”  
Noncompetitive antagonist at the glutamate—aspartate (NMDA) receptor which mechanism is believed to be responsible for mind-altering effects and toxicity (behavioral aberrations, nystagmus, ANS stimulation) - note growing body of evidence suggests that deficits in glutamatergic function may underlie pathophysiology of schizophrenia  
([www.cc.nih.gov/ccc/annualreport97/clinical\\_research/Anesthesiology.html](http://www.cc.nih.gov/ccc/annualreport97/clinical_research/Anesthesiology.html))

### **Partial agonist**

- Agent has some affinity and some efficacy
- May antagonize action of other drugs with greater efficacy
- Antagonists may share some structural similarity with agonists

Examples: pentazocine (Talwin), butorphanol (Stadol)  
Both have mixed agonist/antagonist properties at opiate receptors (weak narcotic antagonist)

Note: both of these drugs have significant toxicities, addictive potential and considerably less effectiveness than opioids hence their use for pain relief is not as common as it once was

### **Drug Referencing: Key Concepts and Terminology** (terms used in PDR, drug handbooks, etc.)

**Therapeutic class:** refers to the drug class or general category to which drug belongs

Examples: antihistamine, antihelminthic, antihypertensive, ACE-inhibitor, etc.

Note: knowing to which class a particular drug belongs provides information regarding its characteristics since drugs of the same class have very similar characteristics. For example, knowing that an unfamiliar drug is a calcium channel blocker would provide a wealth of information about expected effects (and side effects) in the body. For this reason students pursuing pharmacology study drug classes

**Indications** - appropriate clinical reasons to prescribe (or administer) the drug

**Approved Indications:** clinical uses of a drug which have been FDA-approved

Example: alendronate (Fosamax) to improve bone mass in osteoporosis

Example: Flurazepam (Dalmane) to treat insomnia

**Unapproved (off-label) indications:**

Clinically accepted uses of a drug which have not been formally approved by FDA (based on scientific evidence submitted to FDA for drug approval)

Example: use of imiquimod (Aldara) to treat plantar’s wart (it is FDA approved for genital warts but commonly used - with success - to treat other skin conditions)

Note: the FDA does not permit drug representatives to discuss off-label uses of drugs however health care professionals may discuss, prescribe and administer drugs for off-label indications

**Dosing:** appropriate amount and frequency to prescribe and administer a drug

Dosing is usually expressed as an initial dose, usual dose and maximum dose for a particular compound. Sometimes expressed as a total daily dose to be given in divided doses e.g. bid, tid, qid

Dosing is usually given for both adults and children; often pediatric dose must be calculated as a function of weight

Example: fosinopril (Monopril) "Initially 5 mg once daily; Maintenance 20-40 mg once daily"

Example: sertraline (Zoloft) "initially once daily; increase after 1 week to 50 mg once daily; titrate prn at intervals of at least 1 week; maximum 200 mg once daily"

Example lorazepam (Ativan) "given in 2 or 3 divided doses; initially 2-3 mg daily"

Example: amoxicillin for children "children > 3 months .... 25 mg/kg/d in divided doses every 12 hours or 20 mg/kg/day in divided doses every 8 hours"

#### Example of Calculating Pediatric Dosing for Amoxicillin

PDR reads "20 mg/kg/d in divided doses q 8h"  
For child weighing 38 lbs - calculate as follows

1. Convert lbs to kg via dividing by 2.2 where  $38/2.2 = 17.3$  kg
2. Calculate mg/kg/d via multiplying where  $20 \times 17.3 = 346$  mg/kg/day
3. Divide mg/kg/d by number of doses needed - in this case divide by 3 for q 8h where  $346\text{mg}/3 = 115$  mg
4. Dosing is amoxicillin 115 mg q 8 hrs - Doctor's order should be in this range \*

\* Dosing need not be exactly the same but should not vary markedly from calculated range particularly where medication is toxic (amoxicillin is not toxic)

Note: nurses should NOT administer dosing which exceed maximum recommended dosing without clarifying the order with prescriber. If dose far exceeds recommended dosing and prescriber insists it is correct, nurse should refuse to administer a dose he/she believes is harmful - example Demerol 500 mg IM q 4-6 h prn (usual dose is 50-100 mg) should not be administered. Nurses accepting and acting on verbal orders in such instances are on particularly precarious grounds.

Note: different routes of drug administration can have vastly different recommended dosing for some drugs - esp if there is extensive first pass effect. Other drugs remain constant regardless of route

Example: meperidine (Demerol) 50 mg IM equals meperidine (Demerol) 200 mg PO

Example: thiamine 100 mg IM equals thiamine 100 mg PO

**Contraindications:** clinical situations wherein drug should NOT be prescribed or administered

Example: cefditoren (Spectrocef) is contraindicated for “milk protein allergy (not lactose intolerance). Carnitine deficiency or conditions causing carnitine deficiency”

This drug should NOT be prescribed or administered to persons with milk protein allergy or carnitine deficiency.

Example: Trimethoprim/sulfamethoxazole (Bactrim) is contraindicated for “megaloblastic anemia due to folate deficiency, 3<sup>rd</sup> trimester pregnancy (Cat C) ....nursing mothers of ill, stressed, G6PD-deficient, premature, or hyperbilirubinemia infants

This drug should NOT be administered to persons with folate deficiencies resulting in megaloblastic (high MCV) anemia. Similarly, it is NOT to be administered to women with 3<sup>rd</sup> trimester pregnancies or women nursing certain infants

Example: benazepril (Lotensin) is contraindicated for history of ACEI-associated angioedema, pregnancy (Cat D) in 2<sup>nd</sup> and 3<sup>rd</sup> trimester.

ACE-inhibitor-associated angioedema (swelling of the lips) can result in anaphylaxis (and associated fatality) with subsequent dosing. Obviously it is NOT appropriate to administer the drug to such patients. Similarly, administering the drug to pregnant women can result in agenesis (failure to develop) of the kidney in the fetus which would in turn result in fetal demise.

Note: the fact that a drug was ordered would not exonerate a nurse who administered the drug to a patient for whom the drug was contraindicated. The nurse would be held liable (as would the prescriber) in such case

**Precautions** - less absolute than contraindications.

- Use caution but may be given in certain circumstances
- Precautions identify situations wherein the drug must be given with caution

Example: Biaxin - PDR reads as follows:

Contraindicated: cisapride, pimozide

Precautions: Severe renal impairment, pregnancy (Cat C): usually not recommended. Nursing mothers

Interpretation: This drug absolutely may not be given to a patient who is also receiving cisapride (Propulsid) or pimozide. Cisapride is now withdrawn from the market but the principle remains. By contrast, it may be given with severe renal impairment but only with caution i.e. with a greatly reduced dose. As for the pregnancy, while it is not recommended (and generally not ordered or administered), giving it is not an absolute prohibition (albeit a poor idea). By contrast, giving an ace-inhibitor agent - e.g. benazepril (Lotensin) - to a pregnant women is absolutely inappropriate (doing so is contraindicated) and would result in fetal demise. It would also probably result in a law suit indicting both the prescriber and the person who administered the drug.

**See “Perinatal and Pediatric Pharmacology”**

**Interactions** - Drugs or food which may interfere with effectiveness or cause toxicities

- Certain drugs interfere with the absorption or action of other drugs
- Certain drugs are toxic in combination with other drugs
- Certain drugs are inactivated by food

Example: captopril (Capoten)

Co-administration with potassium supplements or potassium-sparing diuretics can easily result in hyperkalemia. This combination must be avoided

Example: alendronate (Fosamax)

Drug must be taken with 8 oz water on an otherwise empty stomach. Any food or beverage for 30-60 minutes will prevent its absorption

Example: tetracycline or doxycycline (Vibramycin)

Milk products taken within 1-2 hours of this drug will inactivate it.

Example: phenytoin (Dilantin)

This drug is quite toxic and highly protein bound. Other protein bound drugs can "bump" dilantin from albumin binding sites resulting in higher free drug level and subsequent toxicity

Example: sucralfate (Carafate)

Avoid within 30 minutes of antacid dosing. May reduce absorption of tetracyclines, phenytoin (Dilantin), cimetidine (Tagamet), digoxin (Lanoxin), ciprofloxacin (Cipro)

Nurses are responsible to avoid drug interactions particularly where there are multiple prescribers (as is common in hospital setting). Nurses should alert prescribers of potential interactions as one prescriber may not be aware of what others are ordering. Similarly nurses are responsible for the time doses are administered and accordingly must schedule dosing to avoid known interactions with respect to meals or other medications

**Adverse Reactions** - side effects of drug administration

- Undesirable responses - can range from mild to fatal
- Usually predictable; many cases unavoidable - significant problem  
Many limit use of otherwise therapeutic agent  
Example: anticholinergics while effective in treating GI hypermotility are suitable only for short term use due to extensive side effect profile
- Intensity often dose dependent
- May be immediate or delayed reaction
- Prescriber and nurse can advise re strategies to avoid side effects
  - Ice chips for dry mouth, rise slowly to avoid dizziness
  - Clients should be counseled re most common effects
- Sometimes pharmacologic interventions required to deal with side effects  
Laxatives, anti-emetics

Example: opioids (morphine, codeine) commonly produce sedation, drowsiness, constipation at usual or prescribed dosage

Example: Beta blockers - impotence, fatigue and depression

Example: Anticholinergics - dry mouth, urinary retention and sedation

### **Idiopathic adverse reaction**

- Unpredictable - not related to dosing
- Affects only a small percentage of persons treated with the drug
- Types of idiopathic responses
  - Overresponse or abnormal sensitivity to a drug
  - Under-response or abnormal tolerance to a drug
  - Qualitatively different effect from what is expected  
Example: excitation after administration of sedative
  - Unpredictable, unexplainable symptoms  
Example: Hepatic failure with troglitazone (Rezulin)
- Result from genetic enzyme deficiencies -> abnormal drug metabolism

### **Allergic reactions**

- Altered state of reaction to a drug
- Results from previous sensitizing exposure -> immunoglobulins  
**IgE, IgM, IgG**
- Subsequent exposure to antigen -> allergic response
  - **Histamine** release
  - Edema, prostaglandins, swelling, erythema, pain, pruritus
- Each subsequent exposure tends to be worse than previous
- Systemic (anaphylaxis) vs local reaction
  - Systemic: generalized symptoms - frequently life-threatening
  - Local reaction: symptoms limited to site of exposure
- **Anaphylaxis: hives, laryngeal edema, pulmonary edema, hypotension**  
Most extreme form of systemic reaction  
Requires immediate intervention: **epinephrine, antihistamines**  
Bronchodilators, IV steroids, sometimes H2-blockers
- Treatment allergy: **antihistamines - steroids**

### TYPES OF ALLERGIC REACTIONS

#### **Type I (anaphylaxis) - immediate, life-threatening**

- Mediated by IgE
- Bronchospasm, hypotension, vasospasm, rapid death

#### **Type II (cytotoxic reaction)**

- IgG, IgM
- Also known as autoimmune response
- May take several weeks to resolve
- Common predisposing drugs
  - Hemolytic anemia: methyldopa (Aldomet)
  - Thrombocytopenia: quinidine (Quinaglute)
  - Lupus erythematosus: procainamide (Pronestyl)

#### **Type III (Arthus reaction or "serum sickness")**

- Occurs 1-3 weeks after exposure
- Forms IgG
- Manifestations:
  - Vessel, angioedema, arthralgia, fever, lymphadenopathy, splenomegaly
- Common predisposing drugs

Penicillins, sulfonamides, phenytoin (Dilantin)

**Type IV - cell-mediated or delayed hypersensitivity reaction**

- Direct skin contact and sensitized cells -> inflammation
- Involves sensitized T lymphocytes and macrophages
- Example: Poison ivy dermatitis

Note: It is never appropriate to administer a drug to a patient with a known allergy to that drug. Each episode manifests with increasing severity. For example: a patient with a minor allergic skin rash could have anaphylaxis on subsequent exposure.

**Pharmacodynamics-pharmacokinetics: Key Concepts and Terminology**

**Tolerance** - decreased physiologic response which occurs after repeated administration

- Increased dosing necessary to achieve therapeutic effect
- Term is not synonymous with addiction or drug-seeking behavior

Tolerance is a physiologic response which occurs in virtually everyone who takes certain drugs (example: opioids). The person may or may not also have addictive or drug-seeking behavior associated with taking the drug. Criteria for establishing drug-seeking behavior are not dependent on physiologic tolerance.

- Common drugs exhibiting tolerance  
Alcohol (ETOH), opium, nitrates

**Cross-tolerance:** tolerance which develops at same receptor site to similar drugs

Example tolerance to effects of barbiturates often results from a cross-tolerance to patients who are heavy users of alcohol (ETOH). Accordingly patients who drink large amounts of ETOH will need larger than usual amounts of barbiturates to achieve the same effect

**Tachyphylaxis:** Quickly developing tolerance after repeated administration of a drug

- Rapid in onset
- Client's initial response cannot be reproduced even with large doses

Example: nitroglycerine (NTG) patch - requires intermittent dosing schedule  
Usually off HS for 8-10 hours to avoid tolerance

**Cumulative Effect**

- Previous dose is not fully metabolized before next dose is administered
- Can occur when drugs excreted more slowly than absorbed
- Each dose adds more than is lost via excretion
- High concentration -> potential toxicity occurs

Example: ETOH intoxication occurs where person drinks faster than can be metabolized

- Rapidly develops; effects readily apparent
- Metabolism rate varies with individual and gender (males more efficient)
- Regular ETOH consumption increases efficiency via increasing enzyme \*  
\* acetaldehyde dehydrogenase converts ETOH to acetaldehyde

Example: Lead poisoning - insidious - prolonged effect with accumulation

### **Drug Dependence**

- Preferred term vs previous terminology of addiction or habituation
- Terminology: opiate dependence, diazepam (Valium) dependence
- Can be physiologic or psychologic

**Physical dependence:** physiologic disturbance occurs when drug is withdrawn

Example: Delirium tremens (DTs) with ETOH withdrawal

Example: shaking and flu-like symptoms with heroin withdrawal

**Psychologic dependence** - state of emotional reliance on drug to maintain its effect

Manifestation is variable: mild craving to compulsive use

Example: cocaine dependence \*

Note: many substances induce both physiologic and psychologic dependence: caffeine, nicotine, diazepam (Valium) and other benzodiazepines

**Drug Interaction:** effects of one drug are modified by another

Beneficial interactions: probenecid (Benemid) increases blood levels of penicillin

Detrimental interactions:

Aspirin (ASA) increases action of warfarin (Coumadin) -> hemorrhage

**Drug antagonism:** combination of two drugs less than sum of drugs acting separately

Example: antacids significantly decrease effectiveness of fluoroquinolones e.g.

Ciprofloxacin (Cipro) with magnesium-aluminum hydroxide (Maalox)

**Summation:** (1 + 1 = 2)

Combination produces enhanced effect equaling sum of individual effects of each agent

Example: aspirin and codeine = additive pain relief vs when either given alone

Allows lower dosing of each drug minimizing side effects

Example: hydrocodone and acetaminophen 5/325 (Percocet)

**Synergism:** (1 + 1 = >2)

Combination produces enhanced effect which is greater than sum of individual drugs

Example: Ace-inhibitors and HCTZ diuretic - enhanced antihypertensive effect

Each lowers BP by different mechanism - combined effect produces

greater decrease in BP than if either given alone.

**Potentiation** - one drug increases effect of the other

Example: caffeine enhances pain relief with NSAIDs or ASA

Example: hydroxyzine (Vistaril) potentiates analgesia of meperidine (Demerol) \*

\* some authorities dispute this notion however it is widely held

## Important Nursing Implications for Medication Administration

*Nurses are professionally, morally legally and personally responsible for every dose of medication they administer.*

Any drug not already known should be “looked up” before administering - no exceptions!

PDR, Mosby GenRX  
Drug handbooks  
Package inserts  
Computerized data base  
Pharmacist consultation

Where information is not available nurse should call pharmacist for information

Nurses are expected (society and courts of law ) to be patient advocates  
- Nurses expected to question orders which appear inappropriate  
- Following authority or intimidation are not acceptable excuses in US

Under what circumstances can nurses administer medications?

Nurses may NOT administer medications to patients without a valid order. It makes no difference whether the medication is a prescriptive or an over-the-counter medication. Similarly, nurses may not legally advise patients to take medications already in their possession where those medications have not been legally prescribed. Example: A patient has left-over medication from amoxicillin prescribed for Lyme Disease. A nurse who suspects that a patient has a strep throat may not legally advise the patient to take this medication to treat the strep throat

Criteria to legally administer medications

1. Medication order must be valid
2. Prescriber must be licensed and prescribing within state regulations
3. Nurse must know purpose, action, effects, major toxic effects, required teaching

What is a valid medication order?

- Identifies patient's name and the date the order is written
- Order leaves no room for doubt re: medication, dosage, route, dosing interval
- Identifies prescriber and includes prescribers signature
- Wording is correct, complete, legible and clearly understandable
- Prescriber is licenced to prescribe within the state and in compliance with statutes
- Anything which is not clear must be **clarified and validated**
- **Changing an order by modifying any part without consultation with prescriber is illegal**

Who can issue medication orders?

**Licensed physicians, dentists, nurse practitioners and physician assistants** may issue orders (prescriptive practice laws will vary by state). No one else may issue orders and in particular not medical students and unlicensed interns. NPs and PAs may have restrictions to prescriptive practice which vary with state

## Responsibilities of nurses administering medication

- **Question drug order** which is unclear or appears harmful
- **Refuse to administer drugs** if reason to believe it will be **harmful**
- Observe and chart drug effects
- Use correct techniques and precautions
- Keep current knowledge base
- Nurse responsible to note physical characteristics of drugs before administering them  
Signs of spoilage, discoloration, precipitates, foreign bodies in solution
- Nurse responsible to note **expiration date**
- Nurse should check for any **patient allergies** prior to administering drug
- Observing and **reporting side effects** and adverse **events** (document actions taken)
- Observe for and document therapeutic response (or the lack of it)

Note: the fact that the nurse has an order to administer a medication which could judgement would dictate otherwise will not protect the nurse. Nurse would be held to the standard of a "reasonable nurse." A reasonable nurse would look up the drug before administering it. If doing so would reveal an obvious error e.g. an order for IV administration when, in fact, the drug is only approved for IM injection, then the nurse would be held accountable for administering it. If, by contrast, the nurse checks everything carefully and administers the drug correctly where subsequently the patient has an unexpected drug reaction, the nurse would not be held liable.

## Are telephone orders (T/O) and verbal orders (V/O) valid?

Written orders are always preferable and should be used unless the clinical situation makes such impractical or impossible e.g. emergencies, intraoperative conditions, etc. Telephone and verbal orders are legal, however, written orders are the safest avenue to protect both the patient and the nurse. Different clinical agencies and hospitals have varying policies regarding whether and under what circumstances nurses can accept verbal/telephone orders.

### **Poor nursing practice to accept T/O and V/O except in emergencies**

- Prescriber may forget to later sign order making legal status questionable
- Verbal orders can be misunderstood or denied by prescriber

Many hospitals have policies which limit T/O and V/O to emergency situations

## Special considerations for IV or other parenteral administration

- Trend is for pharmacist to pre-mix IV medication mixtures  
Also known as IV "**piggyback**" or "add-a-line" or IV solusets (**IVSS**)  
Pharmacist calculates dose and prepares the medication (usually in 100 IV bag)  
Nurse "hangs" medication i.e. connects it to IV tubing
- Nurses may legally prepare IV mixtures but hospital policy may regulate same
- Hospital policies vary regarding whether nurses can administer "**direct push**" IV meds
  - Small quantities of undiluted meds for direct IV injection or into IV tubing
  - Special training and additional certification may be required
- Hospital policies will vary concerning 'high-tech" medication administration
  - Morphine and other opioid pumps
  - Refilling drug reservoirs for epidural analgesia

Can nurses refuse to carry out a valid order?

- Nurses are required to refrain from administering any medication they believe is incorrect or harmful
- Having an order does not absolve the nurse from liability or lawsuit
- Physicians cannot absolve nurse by “taking full responsibility”

### The Five Rights of Medication Administration

1. The *right medication*: the one that is prescribed and that is not contraindicated
2. The *right patient*
3. The *right dose* as is prescribed and as is appropriate
4. The *right route*, form of drug and administration technique
5. The *right time* for the dose (usually within ½ h of scheduled dose) at appropriate intervals

Examples of actual patient injury/death where nurse failed to follow one of the “rights”

1. *Right medication*: Infant died when given injectable form of digoxin instead of pediatric elixir (right medication)  
Nurse was sued for malpractice resulting in a judgement for the plaintiff
2. *Right route*: Texas Infant died when given procaine penicillin IV instead of the ordered IM  
Nurses involved were *criminally prosecuted* for this error
3. *Right patient*: Newark Beth Israel nurse, working a double shift, failed to check armband, administered drug (blood) to wrong patient who subsequently died of hemolytic anemia  
  
Patient who had previously been in that bed was transferred to a different cubicle in the CCU. Subsequently a different patient was in the same bed and the nurse did not check the armband prior to administering the drug. Error resulted in fatality for patient and *criminal prosecution* (and conviction - 10 yr prison sentence) for nurse who also attempted to cover-up the error.
4. *Right dose*: Patient is given 2.5 mg of digoxin instead of 0.25 (right dose) -> digoxin toxicity
5. *Right time*: Patient is given chemotherapy via IV drip over the wrong time interval and it results in renal failure from toxicity (right time)

Nurse was floated to oncology unit wherein she was unfamiliar with medications and protocols. She erroneously administered chemotherapy over 8 hours instead of over the one hours which was ordered believing that slow administration was safer. In fact, the failure to follow the order resulted in renal toxicity and subsequent failure since the medication needed to be flushed with one liter of fluid to avoid toxicity. This nurse also violated another safe practice principle in that she administered a medication regarding which she was unfamiliar.

### Administration vs dispensing medications

Nurses may administer but not dispense medications. Dispensing requires a pharmacist's license. Accordingly, **nurses may NOT label, re-label or combine bottles**, vials, packets of medication. Doing so constitutes practicing pharmacy without a license. Nurses may take medication from stock bottles to administer. They may NOT create stock bottles or modify existing stock bottles.

## Checking medications before administration

Traditionally nurses read medication labels 3 times before administering

- When taking drug container from storage place
- When preparing the dose
- When returning medication to container to storage place

Unit dosing has changed this tradition somewhat but has not changed the fact that nurses must carefully read label before administering drug

**Nurses classically taught to administer only those doses which are self-prepared !**

## Other tips for safe medication administration

1. After calculating doses, **compare the calculated dose to the “reasonable test”**

For example the order is to administer 65 mg of Medication A and the label reads 100 mg/ 5 ml. The dose calculated administered should be somewhat more than 2.5 ml (which is half of 5 ml) because 65mg is a bit more than half of 100 mg. The actual value calculates to 3.25 ml which seems reasonable. A calculated values of e.g. 7.5 ml or 13.0 ml would not be “reasonable” by this logic and should tip the nurse off that something is wrong with the calculation

2. Avoid distractions when calculating drug doses - check, and check again! Do not allow others to interrupt or distract when calculating drug doses. Where interruptions are unavoidable (emergency occurs) redo the calculations
3. Take seriously any comment by the patient who questions the drug or it's size, color, dose and/or a possible allergy. Many errors are averted by patients who are familiar with their medications or routine. **Do not summarily dismiss patient concerns and comments**
4. Record medication dose immediately after administering it
5. Compare information on medication Kardex or computer print-out sheet with prescribers order and medication chart to prevent errors (wrong dose, double dose, wrong medication, etc.)
6. Check armbands routinely
7. **Look up all unfamiliar meds** - never administer an unfamiliar med without looking it up. Doing so is an invitation to a malpractice suit.

## Legal Aspects of Pharmacology and Medication Administration

### Legend Drugs aka prescription drugs

Clarified per Durham-Humphrey amendment (1952) to the federal Pure Food and Drug Act (1906)

"Caution: Federal law prohibits dispensing without prescription"

Drugs classified as legend drugs

- All drugs given by injection (exception insulin)
- Drugs not safely administered unless under supervision of licensed practitioner
- New drugs limited to investigational use - unsafe for unsupervised use

### Over-the Counter Drugs (OTC)

- Drugs available to the public without a prescription
- OTC drugs have potential health hazards
  - Excessive or inappropriate dosing
  - Drug interactions
  - Underlying pathologies
- Many people falsely assume there are no risks
- OTCs can cause significant (and potentially dangerous) drug interactions
  - Other OTCs
  - Prescription drugs
- Medication history must include OTCs (many patient's forget to mention them)
- Some drugs have status change from RX to OTC (often at different dosing)

### Narcotic and Substance Abuse Laws

Harrison Narcotic Act (1914) first law directed toward curbing addiction

- Established the word "narcotic" as legal term
- Regulated importation, manufacture, sale, use addictive drugs \*
  - Cocaine and derivatives
  - Morphine and derivatives
  - Marijuana and derivatives

\* Previously cocaine, morphine, etc. available legally without prescription (Lydia Pinkham solution for "women's problems", laudanum), and also in soft-drinks (Coca Cola)

Comprehensive Drug Abuse Prevention and Control Act (1970) -

- Also known as **Controlled Substances Act (CSA)**
- Provides for research and treatment of drug dependency
- Regulates administration, manufacture, distribution, dispensing
- Directed toward **controlled substances**
- Classification system - according to potential for abuse
- Drugs classified into levels or Schedules from I to V

**Drug Enforcement Administration (DEA)** - 1973

Sole legal drug enforcement agency in US

### Schedule of Controlled Substances

CHARACTERISTICS	DISPENSING RESTRICTIONS	EXAMPLES
I - High abuse potential - No acceptable medical use - Research, analysis only	Approved protocol is necessary	Heroin, marijuana, tetrahydrocannabinols (THC), LSD, mescaline, peyote, psilocybin, methaqualone
II - High abuse potential - Acceptable medical use - Severe physiologic or psychologic dependence	- Written signed RX - No refills allowed - Container warning label *	Opium, morphine, hydrocodone, methadone, secobarbital, pentobarbital, dextroamphetamine, methylphenidate, cocaine
III - Less abuse potential vs II - Accepted medical use - Moderate/low physical dependence or high psychologic dependence	- Written or oral RX - RX expires in 6 mo - No more than 5 refills - Container warning label *	Combo preps with limited opioid, or opioid in combo with non-controlled substance: acetaminophen with codeine (Tylenol w codeine) aspirin with codeine (Percodan)
IV - Lower abuse potential vs III - Accepted medical use - Limited physical or psychologic dependence	- Written/oral RX - RX expires 6 months - No more than 5 refills - Container warning label *	Phenobarbital, chloral hydrate, meprobamate, diazepam (Valium), alprazolam (Ativan) and other benzodiazepines, propoxyphene (Darvon), pentazocine (Talwin)
V - Lower abuse potential vs III - Accepted medical use - Limited physical or psychologic dependence	Written RX or may be OTC (variable state law)	- Limited amounts opioids - Anti-diarrheal, anti-tussives - Guaifenesin with codeine (Robitussin AC) terpin hydrate, diphenoxylate and atropine (Lomotil)

\* Warning label: "Federal law prohibits transfer of this drug to any person other than the client for whom it was prescribed"

## Possession and Administration of Controlled Substances

- Unlawful to possess controlled substance unless one of the following
  1. Obtained via valid RX or order
  2. Pursuant to actions in course of professional practice
- Federal offense to transfer substance to person other than for whom it was RX'd
- Must be inventoried and managed with accountability
  - Pharmacists, physicians, nurses
  - Records re distribution, flow, inventory
- Institutions have policies for strict recording, checking quantities at hand
  - Balance on hand, supplies added, doses administered
  - Usually requires double signature for each step in process
- Stored in double locked cabinet - keys in custody of licenced personnel

### Implications for nursing practice

- Narcotics keys in possession of a nurse at all times
- Keys may transfer from one nurse to another but never left unattended
- **Actual count of all substances** performed beginning and end each shift
- **Double signature** for verification of count - two nurses count
- Each dose administered is signed by two nurses
- "Wasted" doses also signed by two nurses
  - Partial doses administered to comply with order
  - Breakage or outdating RX
- Computerized locked cabinet may eliminate the need for counting

## Brand vs Generic Drugs

- Drugs are labeled by chemical name (generic name) and proprietary name (brand)  
Example: ceftriaxone - generic name; Rocephin: brand name
- Correct format as follows: generic (Brand); example: omeprazole (Prilosec)
- Manufacturer holds patent (exclusive right) to produce drug for specified no of years
- Off-patent drugs may be manufactured by other companies as generics
  - Generics are chemically and pharmaceutically identical to brand
  - Generics are generally more cost-effective and equally efficacious

### Substitution laws: virtually all states have laws regulating substitution

- Most states permit or mandate substitution by pharmacist where available
- Permissive states: prescriber must authorize substitution on RX
- Mandating states: substitution automatic unless prescriber requests otherwise
- Where prescriber does not want substitution, it is noted on RX or order
  - "Dispense as written"
  - "Brand necessary" or "medically necessary"
- Nurse may administer generic substitution unless order states otherwise

### Hospital formularies

- Hospital pharmacy dispenses limited number of drugs i.e. formulary
- Committee develops approved drugs for inclusion in formulary
- Generics used unless contraindicated or not available
- Pharmacist clarifies and interprets orders to be consistent with formulary
- Revised order is recorded on chart for subsequent transcription by nurse

## Types of Drug Orders

**Routine Order** - most common type of drug order

- Drug administered at regular intervals until formal discontinuation
- Methods for formal discontinuation of routine order
  - A subsequent order is written terminating the medication
  - Original order specifies termination date
  - Automatic stop order per some institutional policies
    - Rationale is to require prescriber to reevaluate patient's condition
    - Particularly common with controlled substances and antibiotics

Example: "Amoxicillin 250 mg IVSS q8h"

### PRN order

- Drug to be administered according to client need
- Criteria may be specified
- Within criteria, administered per judgement of nurse
- Most PRN medications for pain

Example: "Demerol 50 mg and Vistaril 50 mg IM q4h prn pain"

### Single order

Drug to be administered once at time indicated

Example: preop medication - "Robinul 0.2 mg IM on call to OR"

OR will call and advise nurse re: time to administer drug usually an hour or so before patient is scheduled for surgery

**Stat Order** - drug to be administered as single dose immediately

Example: "Haldol 10mg IM stat"

Sometimes written as "now" versus "stat" which has somewhat less urgency

Example: "Milk of Magnesia 30 ml now"

**Protocol** - set of criteria which serves as directive under which medication may be administered

#### Standing orders

Officially accepted set of orders (not only meds) applied routinely to patients with certain conditions or under certain circumstances

Example: Admission orders for CCU

1. Admit to CCU
2. 2 gm Na cardiac diet
3. D5W to KVO
4. EKG stat and q am
5. Etc.

#### Flow diagram protocols

Guidelines for treatments and meds based on client variables

Example: sliding scales for insulin administration

Flow diagram protocols

## Transcribing Medication Orders

Transcribing medication orders involves copying orders from the order sheet to the **Medication Administration Record "MAR" or "Medex"**

Purpose: to facilitate the administration of medications by nurses assigned to the patient

Hospitals and agencies will vary regarding specifics of transcribing; some policies may differ from information presented here.

Many agencies have computerized the process including the MAR printout

### GENERAL RULES AND PRINCIPLES OF TRANSCRIPTION AND SUBSEQUENT ADMINISTRATION

1. Transcribing nurse dates and initials entry on "Medex." Order is copied onto "Medex" in the appropriate spaces. Some agencies require 2 nurses to check and initial order before medication can be given. **Use only agency-approved abbreviations.**
2. Nurses who subsequently administer the medication, document doing so on the MAR via indicating date/time of administration and initialing the entry.
3. MAR has sections for routine ongoing orders, single orders and prn orders. In each case, date, time and nurse's initials document each dose given
4. MAR have a section where the nurses enter their initial's followed by their signature such that initials on the MAR can be matched with signatures for purposes of identification
5. When medications are discontinued (D/C'd) the nurse transcribes this order by writing D/C under the original transcription date and initials followed by the date med was stopped and the transcribing nurse's initial's. Any unused (future) spaces are X'd out to prevent inadvert medication administration after the discontinuation date. Often the entire entry for medications which have been D/C'd are marked with a yellow highlighter such that they will stand apart from active ongoing orders.
6. Medication entries can be recopied and/or re-timed as may be needed when the card is filled or a new administration schedule is needed. The latter situation may exist so as to correct for a missed dose, avoid interactions with a new medication, administer at a more convenient or preferable time, etc. There are a variety of reasons why a medication may be re-timed. When re-timing or recopying an entry, mark the original as such and X-out any remaining spaces to avoid someone inadvertently administering the medication. Next, the medication is re-entered on an unused place on the Medex" In all cases, the original entry is marked as recopied or re-timed. The medication which is being recopied or re-timed is then recorded on an unused portion of the "Medex" to include the date and the initials of the person recopying the medication. Often the old entries are marked with a highlighter so they stand apart from active medication orders.
7. Hospitals typically use standard times to schedule medications. See "Common Medication Administration Times." Where appropriate, the standard timing schedule is used, however, there is no absolute rule which requires a specific time unless the order so specifies. In fact, some medications must be administered at times other than the standard so as to avoid drug-food interactions. The "MAR" typically has spaces for up to QID dosing. If the medication is to be administered more frequently than QID - e.g. q 2h - simply use more than one unit (section) on the "MAR."

**COMMON STANDARD PHARMACEUTICAL ABBREVIATIONS AND SYMBOLS**

ac	before meals	ō	no or none	T/O	telephone order
ad lib	freely	OD	right eye	tsp	teaspoon (5 ml)
bid	twice each day	OS	Left eye	U	unit
ĉ	with	OTC	over the counter	V/O	Verbal order
caps	capsule	OU	each eye	i, ii, iii	one, two, three
D/C	discontinue	pc	after meals	3	dram
elix	elixir	q	every		ounce, fluid ounce
g, gm	gram	qd	every day	X	times
gtt	drops	qh	every hour	>	greater than
hs	hour of sleep	q4h	every 4 hrs	<	less than
IM	intramuscular	qid	four times day	=	equal to
IV	intravenous	qod	every other day	↑ or ↗	increase
IVPB	IV piggyback	qs	sufficient quantity	↓ or ↘	decrease
kg	kilogram	®	right		
circled L	left	Rx	take		
L	liter	š	without		
ug, mcg	microgram	SL	under the tongue		
mg	milligram	SOS	if necessary, one dose only		
mEq	milliequivalent	ss	a half		
min, m	minim	stat	at once		
ml, mL	milligram	SC, SQ	into subcutaneous tissue		
ng	nanogram	tbsp	tablespoon		
NPO	nothing by mouth	tid	3 times per day		

**COMMON MEDICATION ADMINISTRATION TIMES**

qd	10A	q12h	8A - 8P 10A- 10P 12A -12P 2A - 2P 4A - 4P 6A - 6P
bid	10A - 6P	q 8h	8A - 4P -12P 10A - 6P - 2A 12N - 8P -4A 6A - 2P- 10P
tid	10A - 2P - 6P	q6h	8A - 2P - 8P - 2A 10A - 4P - 10P - 4A 12P - 6P - 12N - 6A
qid	10A - 2P - 6P -10P	q4h	6A -10A -2P -6P -10P - 2A

**COMMON MEDICATION ABBREVIATION**

ACE I	ACE inhibitor	EC	enteric coated	MOM	milk of magnesia
ARB	angiotensin receptor blocker	ETOH	ethyl alcohol	6-MP	6-mercaptopurine
ACTH	adrenocorticotropin hormone	Fe	Iron	MS	morphine sulfate
ASA	aspirin	5-FU	5-fluorouracil	Na	sodium
DES	diethylstilbestrol	HC	hydrocortisone	NS	normal saline
DM	dextromethorphan	HCTZ	hydrochlorothiazide	NSAID	nonsteroidal antiinflammatory drug
D5W	5% dextrose in water	INH	isoniazid	NTG	nitroglycerine
D5NS	5% dextrose in normal saline	K	potassium	PAS	
D51/2 NS	5% Dextrose in ½ normal saline	KCl	potassium chloride	PB	phenobarbital
DW	distilled water	LOC	laxative of choice	PNC	penicillin

**TRANSCRIBING MEDICATION ORDERS**

**Lois E Brenneman, MSN, ANP, FNP, C**

**Sample Orders** for 65 year old female admitted with diagnosis of dysfunctional uterine bleeding (DUB). She is pre-op for total abdominal hysterosalpingo-oophorectomy (T-HSO). All medication orders have been transcribed onto the Medication Administration Record (MAR) or "Medex" show below. This form has been computerized in many agencies. All other orders would be transcribed to the "Kardex" or similar record-keeping system which may be computerized in some agencies, as well. .

<b>ST JOSEPH HOSPITAL - KANSAS CITY, MO</b>	
	<b>SMITH, ANITA</b> DOB 10/15/37 M25-3678 Dr. Robert Anderson
<b>MEDICAL ORDERS</b>	
3/4/02	<ul style="list-style-type: none"><li>- Admit East 5</li><li>- DX: DUB - preop T- HSO</li><li>- Activity: OOB as tolerated</li><li>- Diet: Soft</li><li>- IV: D5W KVO</li><li>- Allergy: Sulfonamides</li><li>- Comprehensive metabolic, CBC, U/A, urine C/S, PT/PTT</li><li>- Type and X-match 2 units PC - on call to OR</li><li>- Colace 100 mg PO bid</li></ul> <p style="text-align: right;"><i>R Anderson M.D.</i></p>
3/5/02	<ul style="list-style-type: none"><li>- Amoxicillin 250 mg IVSS TID</li><li>- Endometrial biopsy - Done</li><li>- Transvaginal U/S</li><li>- Old charts to floor</li><li>- Medical Consult Dr Ryan - Pre-op clearance</li></ul> <p style="text-align: right;"><i>R Anderson M.D.</i></p>
3/6/02	<ul style="list-style-type: none"><li>- Feosol 325 mg PO TID</li><li>- EKG and Echocardiogram today</li><li>- CXR</li></ul> <p style="text-align: right;"><i>Michael Ryan D.O.</i></p>
3/7/02	<ul style="list-style-type: none"><li>- Medically cleared for OR</li><li>- MOM 30 cc PO HS</li></ul> <p style="text-align: right;"><i>Michael Ryan D.O.</i></p>

ST JOSEPH HOSPITAL - KANSAS CITY, MO

**SMITH, ANITA**

DOB 10/15/37

M25-3678

Dr. Robert Anderson

**MEDICAL ORDERS**

- 3/7/02
- NPO after midnight
  - Robinul 0.2 mg IM on call to OR 3/8/02
  - Dalmane 30 mg HS

T/O Dr. ~~Forte~~ Jane Zinn, RN

*A. Forte, M.D.* (anaesthesiology)

- 3/8/02
- Renew Amoxicillin 250 IVSS q8h  
Kate Varrow, NP, C

- 3/8/02
- POST-OP Orders
- S/P T-HSO
  - VS q 15 min x 1h -> q 30 min x 1 hr -> q 4h
  - Foley catheter
  - IV: D5NS 100 cc per hr
  - Full fluids tonight; soft diet in a.m.
  - Pad count q 1 hr
  - Demerol 50 mg and Vistaril 50 mg IM q 4h prn
  - Dalmane 30 mg HS prn
  - BR today; OOB in am
  - D/C Feosol
  - Colace 100 mg PO BID
  - Amoxicillin 250 IVSS q 8h

*R Anderson M.D.*

- 3/9/02
- D/C Amoxicillin
  - D/C Demerol/Vistaril

*R Anderson M.D.*

The transcriber should understand the difference between routine standing orders, single orders, stat orders and PRN orders as well as which medication orders above would appropriately be classified in each category.

**SAMPLE "MEDEX" - Side 1**

**MEDICATION ADMINISTRATION RECORD - ST JOSEPH HOSPITAL, KANSAS CITY, MO**

Allergies: Sulfonamides (Rash)

**SMITH, ANITA**

DOB 10/15/37

M25-3678

Dr. Robert Anderson

KEY: D/C (Discontinued) - R (Renewed) - Circled (Med withheld)

Date ordered	Init	Medication	Time	Date 3/5	Date 3/6	Date 3/7	Date 3/8	Date 3/9	Date 3/10
3/5/02 R 3/8  D/C 3/9	RK	<i>Amoxicillin 250 mg IVSS q 8h</i>	10a	RK	gZ	gZ	Ⓚ	RK	X
	AM		4p	MJ	MJ	gZ	EV	D/C	X
	RK		10p	EV	EV	EV	EV	X	X
3/6/02  D/C 3/8	AM	<del>Fend</del> <i>325 mg PO tid</i>	10a		AM	AM	NPO	X	X
	RK		2p		RK	RK	NPO	X	X
			6p		gZ	RK	D/C	X	X
3/6/02 <i>Recopied</i>  R 3/8	MJ	<i>Colace 100 mg PO BID</i>	10a		AM	AM	NPO	RK	
	EV		6p		gZ	gZ	NPO	EV	

RK	Rita King, RN	gZ	Janet Sinn, RNU	Init	DT	Time	SINGLE ORDERS
MJ	Mary Jones, RNC	AM	Am Murphy RN	✓	3/7	10P	MOM 30 c PO
EV	Elizabeth Vicks RN	EE	Eileen Erblich, LPN	EE	3/7	10p	Dalmane 30 mg PO
				MJ	3/8	7a	Robinol 0.2 mg IM

**SAMPLE "MEDEX" - Side 2**

**MEDICATION ADMINISTRATION RECORD - ST JOSEPH HOSPITAL, KANSAS CITY, MO**

Allergies: Sulfonamides (Rash)

**SMITH, ANITA**

DOB 10/15/37

M25-3678

Dr. Robert Anderson

KEY: D/C (Discontinued) - R (Renewed) - Circled (Med withheld)

DT	INIT	PRN Medications	Date Time Initials						
3/7 D/C 3/9	RK	Demerol 50 mg and Vistaril 50 mg IM q4h prn	3/8	3/8	3/9	X	X	X	X
	RK		4P	10P	3A	X	X	X	X
			EV	EV	MJ	X	X	X	X
3/8	AM	Dantrolene 30 mg HS prn	3/9						
			11P						
			EV						
3/9	EV	Percocet 2 tabs PO q 4-6 h prn	3/9	3/9					
			IOA	7P					
			RK	EV					

## Drug Delivery Systems

**Floor Stock System:** rarely used (replaced by unit dosing)

- Medications stored in bulk in medication room of nursing unit
- Pharmacist prepares and dispenses stock bottles
  - Nurses may NOT prepare or alter stock bottles as doing so constitutes practicing pharmacy without a license
- Nurse “pours” meds into individual cups prior to administering to patients
  - “Pours” refers both to liquid meds as well as taking tablets out of a bottle
- Increased potential for error due to large array of stock medications
- Financially and economically unsound
  - Losses due to misplaced or forgotten charges
  - Need for frequent total drug inventories (time consuming)
  - Storage problems - crowded medication rooms
- Virtually all agencies have replaced it with “unit dosing” system
- Used in home care settings

**Unit Dosing** - widely used

- Doses individually packaged usually in foil or blister packages
- Individual packages include brand, generic name, lot number and expiration date
- Pharmacist dispenses correct number of doses for a specified time period to floor
  - Night supervisor normally authorized to dispense meds on 11-7 shift
- Doses are stored in carts (usually wheeled) with drawers for each patient
- Meds administered to patients from the cart which is usually wheeled to each room
- Unused and unopened packages can be returned to pharmacy
- Patient charge slips are usually prepared in pharmacy
- “Borrowing” meds from one patient drawer to another is discouraged
  - Creates errors concerning patient charges
  - Potential errors from no pharmacist participation in process
- Disadvantage: creates delays with new or “stat” drugs
  - Some agencies have “Stat packs” of common meds for this purpose
  - Computerized medication cabinets eliminate the problem
- Pharmacist calculates dosing - increases safety; decreases errors
  - Most IVSS are now prepared in pharmacy
  - Nurses still have occasion to calculate and prepare IV meds
- IVSS usually prepared in “clean room” with filtered air flow

## Calculating Drug Doses

See handout “Medication Calculations”

## PERINATAL AND PEDIATRIC PHARMACOLOGY

Lois E. Brenneman, MSN, ANP, FNP, C

### DRUG THERAPY IN PREGNANCY

- Most drugs taken by pregnant women can cross the placenta
- As much as possible avoid prescribing drug therapy to pregnant women
- Very little research available re: effects of drugs on fetus
  - Most info from animal studies
  - Some info from older drugs with long established safety record
- Risk versus benefits evaluation - prescribe only where benefits outweigh risks
- Examples of appropriate prescribing
  - Control of maternal asthma (anoxia has detrimental effects on fetus)
  - Treatment of maternal infections (certain antibiotics acceptable)
  - Correction of maternal hypothyroidism or diabetes (both essential to well-being of fetus)
  - Prophylaxis influenza vaccine to mother (Risk of influenzae outweighs risk of vaccine)

### PREGNANCY CATEGORIES

#### CATEGORY A:

No demonstrated fetal risk in humans during any stage of pregnancy.

#### CATEGORY B:

No demonstrated fetal risk in animal studies but no adequate studies in pregnant women  
or  
Animal studies have show an adverse effect but studies in pregnant women have no demonstrated a risk during any stage of pregnancy.

#### CATEGORY C:

Animal studies have sown an adverse effect on the fetus but there are no adequate studies in humans.  
or  
No animal studies are available (use of drug may be acceptable despite the risks)

#### CATEGORY D:

Evidence of human fetal risk but the benefits from use of the drug may be acceptable despite the risks.

#### CATEGORY X:

Animal or human studies have demonstrated fetal abnormalities or adverse reaction reports give evidence of fetal risk (risk to a pregnant woman clearly outweighs the possible benefit).

## DRUGS USED DURING LACTATION

### THREE CATEGORIES

#### NO REPORTED EFFECTS:

RX not secreted or concentrations in milk below that known to produce pharmacologic or toxic effect in neonate.

#### USE WITH CAUTION:

Concentrations known to be present in milk are possibly sufficient to produce toxic effect , however, such an effect is considered to be of minimal significance or hazard to neonate.

#### USE IS CONTRAINDICATED:

Drug secreted in milk in sufficient quantities to produce undesired response in neonate; therefore drug should not be administered to nursing mother or mother should discontinue nursing while on med.

Examples: cimetidine, cyclophosphamide, cyclosporine, doxorubicin, ergotamine, gold salts, methimazole, methotrexate, lithium.

### ADDITIONAL LACTATION CONSIDERATIONS

- Most drugs administered to the mother appear in breast milk.
- Often there is a lack of complete information
  - No information relating drug concentrations in breast milk to dose and dose timing.
  - Some information is derived solely from animal studies
  - Reports of toxic effects lack quantity of drug in breast milk or quantity of milk ingested.
- Drugs to be used conservatively during lactation
- Most drugs will enter breast milk although concentration achieved in breast milk is usually low.
- Mother should take drug 30-60 min after nursing and 3-4 hours before next feeding
  - Allows time for maternal drug clearance
  - Facilitates relatively low maternal blood concentration of drug
  - Clearance will be effected by drug half-life
- Most sedatives and hypnotics can produce a pharmacologic effect in infants.
- Opioids can cause drug dependence
  - Methadone requires tapering infant dosing
  - Watch for signs and symptoms of withdrawal
  - Some authorities support breast feeding while mother on methadone \*

\* Koren, G. and Cohen, M.S. (1995). Special aspects of perinatal and pediatric pharmacology. In B.G. Katzung (Ed.). Basic and clinical pharmacology. (pp. 913-922). Norwalk, CT: Appleton and Lange.

## EFFECTS OF COMMON SUBSTANCES

- **ETOH:** Minimal use is not harmful; excessive amounts can produce adverse effects in infant.
- **Nicotine:** low concentrations in breast milk of smoking mothers; no side effects in infants
- **Caffeine:** Very small amounts are excreted in breast milk of coffee-drinking mothers.

## COMMON DRUGS TO AVOID

- **No tetracycline** - permanently stains teeth yellow-brown
- **Lithium:** exposes infant to large amounts of drug; avoid in breast-feeding
- Avoid **propylthiouracil** and **tolbutamide**
- **Isoniazid** may cause neonate to develop pyridoxine deficiency (must supplement mother)
- **Chloramphenicol** can cause bone marrow suppress
  - Concentration is usually not high enough to cause grey baby syndrome
  - Drug is rarely used today due to availability of good alternatives
- **Radioactive diagnostic drugs** (contrast dye, radiolabeled albumin, radioiodine, etc)
  - Can cause thyroid suppression and increase risk of thyroid CA in neonate to 10 fold
  - Important implications in working up postpartum hypo-hyperthyroid presentations
    - Hyperthyroidism is common post-partum and usually self-limiting; resolves
    - If order thyroid scan, mother cannot breast feed for 8 or more months

## PEDIATRIC DRUG DOSING

- Result from differences in pharmacokinetics in infants and children
- Simple proportionate reduction in adult dose may NOT be adequate.
- Consult manufacturer package insert, where available (best source for dosing)
- Approximation can be made on any of several methods based on age, wt, surface areas.
  - Used where manufacturers recommendations not available
  - **Dosing based on surface area is best** (see below) - most likely to be adequate
  - Dosing based on age or weight tend to be conservative.

**Young's rule:** based on Age

$$\text{Dose} = (\text{Adult dose})(\text{Age in years}/\text{Age} + 12)$$

**Clarke's rule:** based on weight (somewhat more precise)

$$\text{Dose} = (\text{Adult dose})(\text{kg}/70) \text{ or}$$
$$\text{Dose} = (\text{Adult dose})(\text{lbs}/150)$$

### DETERMINATION OF DRUG DOSAGE FROM SURFACE AREA

WT KG	LBS	AGE	SURFACE AREA (m <sup>2</sup> )	% ADULT DOSE
3	6.6	Newborn	0.2	12
6	13.2	3 mo	0.3	18
10	22	1 yr	0.45	28
20	44	5.5 yr	0.8	48
30	66	9 yr	1.0	60
40	88	12 yr	1.3	78
50	110	14 yr	1.5	90
60	132	Adult	1.7	102
70	154	Adult	1.76	103

Silver H.K., Kemp, C.H. and Bruyn, H.B. (1983) Handbook of pediatrics 14th ed. Norwalk, Ct: Lange.

EXAMPLE: adult dose is 1 mg/kg; dose for 3 month old infant would be 2 mg/kg (18% of 70 mg/6 kg).

### DRUG ABSORPTION:

- Follows same general principles in infants and children as in adults.
- Unique factors: blood flow at site of administration, gastrointestinal function

## DRUG DISTRIBUTION:

- Body composition changes w development
- Neonate has higher percentage of its body in form of water (70-75%) vs adult (50-60%).
- Differences in water percentage between full term (70%) vs pre-term (85%).
- Extracellular water 40% for neonate vs 20% for adult.
  
- More Important for water-soluble drugs (aminoglycosides) than for lipid-soluble agents.
- Plasma binding proteins: albumin is reduced in neonate -> **higher potential for toxicity**
  - Free concentration of drug is increased -> greater drug effect
  - Can be toxic in spite of normal or even low plasma concentration of total drug
  - Total drug reflects both bound and unbound drug

## DRUG METABOLISM:

- Most metabolism occurs in liver with Cytochrome P450-dependent reactions
  - Mixed-function oxidases (MOF)
  - Conjugating enzymes (CE)
- Cytochrome p450 reactions substantially lower in early neonatal life
- MOF and CE are 50-70% of adult values in early neonatal life.
  
- Drug dosing must be adjusted appropriately
- Hepatic immaturity predisposes neonate to adverse effects hepatically metabolized drugs

## DRUG EXCRETION:

- Glomerular filtration rate (GRF) lower in newborns than older children and adults
- Limitation persists for first few days of life
- Examples reduced drug renal clearance: penicillin, aminoglycoside, digoxin.