Suppositories
Required readings
Ansel: chapter 12
Thompson chapter 23, 31

LEARNING OBJECTIVES

•Be able to describe the anatomy and physiology of the rectum, vagina & urethra
•Be able to describe drug delivery to the above mentioned areas
•Be able to describe the different types of suppository bases and their properties

•Know three (3) and describe 2 methods of suppository preparation.
•Be able to manufacture suppositories with the different types of bases (after the lab)

•Determine the density factor of a drug in different bases

•Describe the proper formulation, packaging, and administration of suppository bases.

History

The "Eber Payrus" 1550 BCE the earliest known "Fertility Control Recipe."
This is one of a compendium of medical inscription left by the indigenous Africans of (Ta-Merry, Ta-Nehisi, Itopi and Meroe).
It is an inscription for medicated "Tampon" designed to prevent pregnancy.
It requires the following: A mixture of the tips of the shrub of Accacia and honey made into a tampon and inserted into the vagina as a suppository.
The chemical reaction is that Accacia fermentation breaks down into lactic acid, one of the active spermicidal agents used in the contraceptive jellies today.

Definition: Suppositories are solid bodies of various weights and shapes, adapted for introduction into the rectal, vaginal or urethral orifice of the human body. They usually melt, soften or dissolve at body temperature.

- *A suppository may act as a protectant or palliative to the local tissues at the point of introduction or as a carrier of therapeutic agents for systemic or local action*

Suppositories

- *local application:*
  - *hemorrhoids, itching, and infections*
- *systemic application:*
  - *antinauseants, antiasthmatics, analgesics, and hormones*

Suppositories are suited particularly for producing local action, but may also be used to produce a systemic effect or to exert a mechanical effect to facilitate emptying the lower bowel.

Rectal Suppository

Effect	Suppository	Comment
Local	**Hydrocortisone supp.**	**For use in inflamed hemorrhoids and other inflammatory condition of the anorectum area**
	Glycerin supp.	**Laxative (by local irritation of the mucous membrane)**
Systemic	**Chloropromazine**	**Tranquilizer**
	Oxymorphone Hcl	**Narcotic analgesia**
	Ergotamine tartarate	**migraine**

Suppositories

- Rational:
  GI, side effects, stability, first pass effect –systemic circulation, by pass portal circulation, unable to swallow, vomiting

Suppositories

- Tissue of rectum different compared to GI tract
- No microvilli
- Vascularization of submucosal region

Rectal Suppositories

- Rectum:
  neutral pH 2-3 mL
  no buffer capacity
- salt form instead of unionized drug (with lipophilic base, hydrophilic base slowly dissolve)
  Octanol/water coefficient.
- Diazepam and Acetaminophen are not good candidates for fatty bases

Suppositories

- *Rectal suppositories are cylindrical or conical in shape, and tapered or pointed at one end. The weight of one suppository is approximately 2 grams and 2-3 cm in length.*
- *Infant suppositories weigh about half as those of adult rectal suppositories.*

Vaginal Suppositories

- **Fibromuscular tub about - 7.5 cm long**
- **Vaginal Blood Circulation**
  - **Blood supply vaginal artery**
  - **Blood return avoids the hepatic portal system**
- **Typically targeted drug administration**
- **Vaginal fluids**
  - **Origin in cervix**
  - **Protective mucus**
- **Complex mixture of proteins and polysaccharides**
  - **Low pH 3**
  - **Prepuberal & post-menopause**
  - **neutral to slightly alkaline**

Suppositories

- Vaginal suppositories, are ovoid or globular in shape, and weigh approximately 3-5 grams each.
- Extemporaneously compounded vaginal suppositories are often compounded with water-soluble bases such as polyethylene glycol or glycerinated gelatin to minimize leakage. (pH4.5)
- Some vaginal suppositories are actually compressed tablets and are called inserts
- Special insert devices
- Fatty bases (consulting)

Vaginal Suppository

Purposes

- **Contraception (spermicide)**
- **Estrogenic substances (restore vaginal mucosa to its normal state)**
- **Combat an invading pathogens *(Trichomonas vaginali, Candida Albicans, Hemophilus vaginalis)***

Anti fungus: nystatin, clotrimazole, butoconazole,…..
Anti bacterial: sulfanilamide, povidone-iodine, oxytetracyclin

Formulation

- **The most common used bases are combinations of PEGs**
- **Surfactants and preservatives are usually added**
- **The formula should be buffered to an acid pH (around 4.5)**

Urethral suppositories

- Tube
  - males 20 cm
  - females 4 cm
- Poorly perfused by blood

Suppositories

- Urethral suppositories are approximately 5 mm in diameter and 50 mm in length for females and 125 mm for males, with a weight of 2 g for females and 4 g for males.

Summary of Suppositories Types

- **Rectal are cylindrical or conical**
  - **approx 2 g, about 2-3 cm long**
- **Vaginal may be ovoid, globular**
  - **3 to 5 g**
- **Urethral vary depending upon male/female**
  - **male 5 mm dia, 125 mm L, 4 g wt**
  - **female 5 mm dia, 50 mm L, 2 g wt**

Desirable properties of suppository bases

- **Stable under normal conditions**
- **Compatible with drug and auxiliary agents**
- **Free from objectionable odor and have an aesthetically appealing appearance**
- **Nontoxic and nonirritating**
- **It shrinks just enough on cooling, Suitable viscosity**
- **Melt or dissolve in the intended body orifice**
- **Mixes with or absorbs some water**
- **Some wetting and/or emulsifying properties**

Suppository Bases

The ideal suppository base should be nontoxic,

- nonirritating,
- inert,
- compatible with medicaments, and
- easily formed by compression or molding.

- As with the ointment bases, suppository base composition plays an important role in both the rate and extent of release of medications.

Suppository Base

- **The base must be able to melt or dissolve**
- Melt: fatty bases, like Cocoa Butter and its synthetic substitutes
- Dissolve: Water soluble/miscible bases (PEG, Glycerin)

Suppository Base

Oleaginous Bases
include
Theobroma Oil
and
synthetic triglyceride mixtures.

Suppository Base

Theobroma Oil or **cocoa butter**
is used as a suppository base because, in large measure, it fulfills the requirements of an ideal base. At ordinary room temperatures of 15° to 25°C (59° to 77°F), it is a hard, but at 30° to 35°C (86° to 95°F), i.e., at body temperature, it melts to a bland, nonirritating oil. Thus in warm climates, theobroma oil suppositories should be refrigerated.

Suppositories

- Cocoa Butter (no emulsifiers)
- 4 modifications (polymorph!)
  - α mp 23 ^{0}C
  - β' mp 28 ^{0}C
  - β mp 34.5 ^{0}C
  - γ mp 18.9 ^{0}C
  - Heating over 38 ^{0}C
  - 1-4 days storage to return into the stable form
  - Testosterone dissolves in CB but not in synthetic bases
  - Phenol, chloral hydrate soften cocoa butter
    - Beeswax, cetyl esters to overcome problem
    - Viscosity!!

Polymorphism

- Polymorphism is important in the development of pharmaceutical ingredients.
- Many drugs receive regulatory approval for only a single crystal form or polymorph.
- In a classic patent case the pharmaceutical company GlaxoSmithKline defended its patent for the polymorph type II of the active ingredient in Zantac against competitors while that of the polymorph type I had already expired.
- Polymorphism in drugs can also have direct medical implications. Medicine is often administered orally as a crystalline solid and dissolution rates depend on the exact crystal form of a polymorph.

Suppository Base

Particular attention must be given to three factors when preparing suppositories with cocoa butter base.

First, this base must not be heated above 35°C (95°F) because cocoa butter is a polymorphic compound and if overheated will convert to a metastable structure that melts in the 25° to 30°C (77° to 86°F) range. Thus, the finished suppositories would melt at room temperature and not be usable.

Suppository Base

The second factor is the change in melting point caused by adding certain drugs to cocoa butter suppositories.

For example, chloral hydrate and phenol tend to lower the melting point. It may be necessary to add beeswax to raise the melting point of finished suppositories back to the desired range.

Third: Coco Butter has no surfactant (can not emulsify water)

Suppository Base

The newer synthetic triglycerides

consist of hydrogenated vegetable oils. Triglycerides from palm,palm kernel, coconut oils (synthetic or semi synthetic)

- Their advantage over cocoa butter is that they do not exhibit polymorphism.
- They are, however, more expensive.
- Some of the bases are single entity formulations.
- Some of the names may denote a series of bases.
- In a series, the bases are varied to give a range of melting points.
- They have better contraction after cooling
- Containing self-emulsifying glycerol monostearate and polyoxyl stearate.

Suppository Base

Fattibase® is a single entity base that consists of triglycerides from palm, palm kernel, and coconut oils.

Wecobee® is a series of bases. Wecobee FS, M, R, and S are all made from triglycerides of coconut oil. But FS has a melting point range of 39.4 to 40.5°C, M has a range of 33.3 to 36.0°C, R has a range of 33.9 to 35.0°C, and S has a range of 38.0 to 40.5°C.

Other triglyceride type bases include Dehydag®, Hydrokote®, Suppocire®, and Witepsol®.

Suppository Base

- Polyoxyl 40 stearate is a mixture of the monostearate and distearate esters of mixed polyoxyethylene diols and the free glycols,
- the average polymer length being equivalent to about 40 oxyethylene units.
- The substance is a white to light tan waxy solid that is water soluble. Its melting point is generally 39° to 45°C

Suppository Base

- Water soluble/miscible bases
- Glycerinated gelatin (70:20:10)
  - Vaginal applications
  - Hygroscopic
  - Moisture before application
- PEG mixtures
  - Should content 20% water
- All water based bases must be preserved!
- Hygroscopicity can cause stinging sensations and discomfort and probably affects the passage of drugs across the mucosa.

hygroscopicity decrease, molecular weight in crease

Suppository Base

Glycerinated Gelatin

is a useful suppository base, particularly for vaginal suppositories. It is suitable for use with a wide range of medicaments including alkaloids, boric acid, and zinc oxide.

Glycerinated gelatin suppositories are translucent, resilient, gelatinous solids that tend to dissolve or disperse slowly in mucous secretions to provide prolonged release of active ingredients.

Glycerin

Glycerin is the simplest trihydric alcohol. It was discovered by Scheele in 1779, who called it the "sweet principle of fats".

Glycerin is the alcohol present in the esters (glycerides) of oils and fats from which it may be released by saponification.

It was more fully investigated by Chevreul who named it "glycerine" and it came into use in medicine and pharmacy about 1846.!

Official USP products include Glycerin Ophthalmic Solution USP, Glycerin Oral Solution USP and Glycerin Suppositories USP

Glycerin is categorized in the NF as a humectant, plasticizer, solvent and tonicity-adjusting agent

Dosage Forms

Glycerin is used in almost every dosage form available today. From a plasticizer in film coatings of tablets, to a solvent, preservative and sweetener in oral liquid dosage forms and in injections. An older dosage form, the glycerogelatins, were actually the forerunner of some contemporary dosage forms containing glycerin.

Suppository Base

- Suppositories made with glycerinated gelatin must be kept in well-closed containers in a cool place since they will absorb and dissolve in atmospheric moisture.
- In addition, those intended for extended shelf-life should have a preservative added, such as methylparaben or propylparaben, or a suitable combination of the two if the water content is higher than the glycerin content.
- To facilitate administration, glycerinated gelatin suppositories should be dipped in water just before use.
- Incompatibility: Gelatin A and B IEP: 7; 5

Suppository Base

Glycerinated Gelatin

is also useful for Urethral suppositories. Such bases contain 60% gelatin, 20% water/ drug and 20% glycerin.

- USP: Glycerinated Gelatin Suppositories
- vehicle consisting of about 70 parts of glycerin, 20 parts of gelatin, and 10 parts of water.
- Glycerinated gelatin suppositories require storage in tight containers, preferably at a temperature below 35 °C.

Rx Glycerinated Gelatin Suppositories

Vehicle-Rectal (100 g)	
Active Drug	qs
Purified water	10 mL
Gelatin	20 g
Glycerin	70 g

Mix the active drug with the water; add the glycerin and mix well. Add the gelatin and heat on a water bath and mix well without incorporating air into the mixture. When the gelatin has dissolved, pour the melted mixture into chilled molds and allow to solidify. Package and label.

Rx Glycerin Suppositories

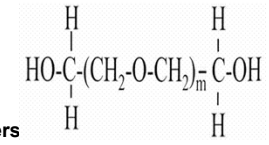
Rectal (105 g)

number depends upon the mold used

- Glycerin 91 g
- Sodium stearate 9 g
- Purified water 5 g

Heat the glycerin in a suitable container to about 40° C. Dissolve the sodium stearate in the heated glycerin. Add the purified water, mix and immediately pour into suitable molds. Cool until solidified and remove, if appropriate. Package and label.

Suppository Base



Polyethylene Glycol Polymers

have received much attention as suppository bases in recent years because they possess many desirable properties.

They are chemically stable, nonirritating, miscible with water and mucous secretions, and can be formulated, either by molding or compression, in a wide range of hardness and melting point.

Like glycerinated gelatin, they do not melt at body temperature, but dissolve to provide a more prolonged release than theobroma oil. .

Suppository Base

- Certain polyethylene glycol polymers may be used singly as suppository bases but, more commonly, formulas call for compounds of two or more molecular weights mixed in various proportions as needed to yield a finished product of satisfactory hardness and dissolution time.
- Since the water miscible suppositories dissolve in body fluids and need not be formulated to melt at body temperature, they can be formulated with much higher melting points and thus may be safely stored at room temperature.

PEG Suppositories

- Labels on polyethylene glycol suppositories should contain directions that they be moistened with water before inserting.
- Although they can be stored without refrigeration, they should be packaged in tightly closed containers.

Suppository Base

Polyethylene Glycol Polymers

MW under 1000 liquids
MW over 1000 solids

Melting points:	300	-15 to -18 °C
	400	4 to 8
	1450	43-46
	8000	60-63

PEG incompatibility

- Oxidation of many drugs
- Phenolic substances complex glycols
- Tannic acid
- Ichthammol
- Aspirin
- Benzocaine
- Vioform
- Sulphonamides

Surfactant Suppository Bases

- Several nonionic surface-active agents closely related chemically to the polyethylene glycols can be used as suppository vehicles.
- Examples of such surfactants are polyoxyethylene sorbitan fatty acid esters and the polyoxyethylene stearates.
- These surfactants are used alone or in combination with other suppository vehicles to yield a wide range of melting temperatures and consistencies.
- One of the major advantages of such vehicles is their water-dispersibility.
- However, care must be taken with the use of surfactants, because they may either increase the rate of drug absorption or interact with drug molecules, causing a decrease in therapeutic activity.

The Suppository Melting Point

It consists of a graduated tube like glass test chamber.

The sample to be tested is placed in a spiral shaped glass test basket inside the test chamber which Itself is surrounded by a heated water jacket

The Suppository Hardness Tester

- An electrically heated chamber containing a sample holder with a number of interchangeable plastic inserts to accept various sized suppositories.

- weights are added in until the suppository collapses.

- The results are expressed in terms of total weight required to bring about the collapse of the suppository.

Suppository Disintegration Time

It consists of 3 Test Stations inside 4.000 ml beakers which are located inside an acrylic glass water bath. The warming solution is heated by an immersion Thermostat

According to the specification the Test Station is turned through 180° every 10 minutes automatically

Suppository Dissolution Testing

Model PTWS-0 is used in a normal dissolution bath. The cell is placed in a normal dissolution vessel.

The stirrer drive is coupled to the horizontally rotating dialysis cell, which contains the suppository.

Active ingredients diffuse through cell membrane and can be measured in the normal way.

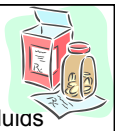
Packaging

- Inert material
- Withstand temperature change and mechanical use
- Protect from radiation
- Protect from microbiological contamination
- Transparent for visual inspection
- Inexpensive
- Space for label
- Facilitate storage

Compounding

- Techniques to compound suppositories
  - Select base
  - Preparation methods
    - Density replacement factor
    - Occupied Volume
    - Double casting method

Base and Drug



- Cocoa butter melts quickly at body temperature, it is immiscible with body fluids and this inhibits the diffusion of fat-soluble drugs to the affected sites.
- Polyethylene glycol is a suitable base for some antiseptics.
- In cases where systemic action is expected, it is preferable to incorporate the ionized rather than the nonionized form of the drug, in order to maximize bioavailability.
- Although nonionized drugs partition more readily out of water-miscible bases such as glycerinated gelatin and polyethylene glycol, the bases themselves tend to dissolve very slowly and thus retard release in this manner.

Drug and Base

- Oleaginous vehicles such as cocoa butter are seldom used in vaginal preparations because of the non-absorbable residue formed
- glycerinated gelatin is seldom used rectally because of its slow dissolution.
- Cocoa butter and its substitutes (Hard Fat) are superior for allaying irritation, as in preparations intended for treating internal hemorrhoids.

Selecting the suppository base

Factors	Fatty bases	PEG
Patient Comfort	More comfortable non irritating	Stinging sensation defecating reflex
Compatibility & Stability	Less reactive melt on storage	More reactive Don't melt on storage
Route of Adm.	Rectal	vaginal
Systemic Effect	Poor release of hydrophobic drugs	More reliable release of hydrophobic drugs
Local Effect	Emollient effect	

Methods of Preparation

(1) Hand Rolling

- Plastic-like mass is prepared by triturating grated cocoa butter and active ingredients in a mortar
- The mass is formed into a ball in the palm of the hands, then rolled into a uniform cylinder
- The cylinder is then cut into number of pieces which are rolled to produce a conical shape

Advantage
- Don't require special equipments
- Avoid necessity of heating cocoa butter

Disadvantages
- Require experience and good technique
- Don't have elegant appearance

(2) Fusion Molding

- First melt the suppository base
- Dispersing the drug in the melted base
- Remove from the heat and pour into a supp. mold
- After congealing, the suppositories are removed from the mold

Advantage
- Have an elegant and professional appearance

Disadvantages
- Caution must be used when heating the base and drug
- Density calculations and mold calibration are required

(3) Compression Molding

Mixed mass of suppository base and drug is forced into a special compression molds

Drug Dose and Volume

- Suppositories are generally made from solid ingredients and drugs which are measured by weight
- When they are mixed, melted, and poured into suppository mold cavities, they occupy a volume - the volume of the mold cavity
- Since the components are measured by weight but compounded by volume, density calculations and mold calibrations are required to provide accurate doses

Density Replacement Factor

• When a drug is placed in a suppository base, it will displace an amount of base as a function of its density.

• If the drug has the same density as the base, it will displace an equivalent weight of the base.

• If the density of the drug is greater than that of the base, it will displace a proportionally smaller weight of the base

• Density factors for common drugs in coca butter are available in standard reference text.

• The density factor is used to determine how much of a base will be displaced by a drug

Density Replacement Factor

$$\text{Density factor} = \frac{\text{Weight of drug}}{\text{Weight of base displaced}}$$

Density factors of drugs in cocoa butter

Aspirin	1.3
Barbital	1.2
Bismuth salicylate	4.5
Chloral hydrate	1.3
Cocaine hydrochloride	1.3
Codeine phosphate	1.1
Diphenhydramine hydrochloride	1.3
Morphine hydrochloride	1.6
Phenobarbital	1.2
Zinc Oxide	4.0

EXAMPLE :

Density Replacement Factor

For example, aspirin has a density factor in cocoa buffer of 1.3

If a suppository has to contain 0.3 g of aspirin, it will replace 0.3 g/1.3 = 0.23 g of cocoa butter

if the blank suppository (suppository without the drug) weighed 2 g, then 2 g-0.23 g = 1.77 g of cocoa butter will be needed for each suppository, and the suppository will weigh 1.77 g + 0.3 g = 2.07 g

So if a pharmacist was making 12 aspirin suppositories using cocoa butter as the base, he would weigh 1.77 g x 12 = 21.24 g of cocoa butter and 0.3 g x 12 = 3.6 g of aspirin

When the Density Factor is Not Known

When bases other than cocoa butter are used, or when the density factor for a drug in cocoa butter is not known. Then the density factor can be

•Experimentally determined by the double casting technique

•Estimated by calculation

Double Casting Technique

• The total quantity of drug is mixed with an amount of base which is inadequate to fill the number of cavities

• The mixture is poured into the mold, partially filling each cavity, and the remaining portion of the cavities are filled with the melted blank base

• The cooled suppositories are then removed, re-melted, mixed and recast to evenly distribute the active ingredient

Double Casting Technique

By recording the necessary information, the pharmacist can determine the weight of base displaced by the drug and then calculate the density factor

Note: a portion of the formula will be lost during this process, so you should always prepare for 2 extra suppositories to ensure that you have enough mixture for the desired number of suppositories.

Calculation the density factor:

The amount of base in the med. supp. = **Weight of the med. supp.** - **Weight of the drug in the supp.**

⇩

The amount of base displaced by drug = **The amount of base in the blank supp** - **The amount of base in the medicated supp**

⇩

$$\text{Density Factor} = \frac{\text{Weight of the drug}}{\text{The amount of base displaced}}$$

Sample Calculation of Density Factor

Using a particular mold, the average weight of a plain cocoa butter suppository was found to be 2.0 g

Using the same mold, cocoa butter suppositories, each containing 300 mg (0.3 g) of drug A, were found to weigh 2.1 g each

Sample Calculation of Density Factor

Weight of suppository made from Coco Butter (A) = 2.0 g

Weight of drug in each medicated suppository (B) = 0.3 g

Weight of suppository with drug and cocoa butter (C)= 2.1 g

$$\text{Density Factor} = \frac{B}{A - C + B}$$

Therefore, density factor of drug A = 1.5

Sample Calculation of Density Factor

Now, knowing the density factor for the drug, the pharmacist can make calculations for a batch of suppositories.

REMEMBER DISPENSING 10 Supp needs 11 or 12

To prepare 10 suppositories:

weight of drug A needed = 10 suppositories x 300 mg/ suppository = 3000 mg = 3.0 g

weight of base needed for plain suppositories = 10 suppositories x 2.0 g/suppository = 20.0 g

weight of base displaced by 3.0 g drug A = 3.0 g/1.5= 2.0 g

Weight of base needed for medicated suppositories = 20.0 g - 2.0 g = 18 g

When the Density Factor is Not Known

When bases other than cocoa butter are used, or when the density factor for a drug in cocoa butter is not known. Then the density factor can be

- Estimated by calculation
- Experimentally determined by the double casting technique

Estimation by Calculation

• One method to determine the density factor of a drug in a base other than cocoa butter required the use of the ratio of a blank suppository of the non-cocoa butter base to a blank suppository of the cocoa butter base.

• This information is generally obtained by calibrating the mold first with one base and then the other base.

• As an example of the method, a mold was calibrated with the PEG base and the average blank suppository weighed 2.24 g.

• The same mold was calibrated with cocoa butter and those blank suppositories weighed 1.87 g on average

Estimation by Calculation

$$\frac{\text{Weight of PEG Sup}}{\text{Weight of Cocoa butter Sup.}} = \frac{2.24\text{ g}}{1.87\text{ g}} = 1.20$$

If 200 (0.2 g) mg of aspirin is to be incorporated into each PEG suppository, it is necessary to determine how much PEG base will be displaced by the aspirin

Estimation by Calculation

That displacement amount can be calculated as follows:

• density factor of aspirin in cocoa butter = 1.3 (from textbook)

• density of PEG base relative to cocoa butter = 1.20 (the ratio obtained from the calibrations)

• 0.2 g of aspirin will displace

0.2/1.3x1.20 = 0.18 g of PEG base

For each PEG suppository to be formulated, 0.2 g of aspirin and 2.06 (2.24-0.18g = 2.06) of the PEG base will be needed

Pharmaceutical Compounding – Nonsterile Preparations <795>

Compounded Dosage Forms
suppositories

- Prepare an excess amount!
- Do not use ingredients that are caustic or irritating and thoroughly comminute solids that are abrasive to the mucous membranes
- Select a base that allows active ingredients to provide the intended local or systemic therapeutic effect
- Reduce solids to the smallest reasonable particle size
- Weight control: 90 -110%

Pharmaceutical Compounding – Nonsterile Preparations <795>

Compounding Process

- ✓ Assessing
- ✓ Calculating
- ✓ Preparing
- ✓ Compounding
- ✓ Observing
- ✓ Checking
- ✓ Signing
- ✓ Cleaning

Summary of Biopharmaceutical and Therapeutic Questions

- **For this drug, will there be adequate absorption by the proposed Route of Administration?**
- **Can you determine how much of each excipient and drug is required?**
- **Will the patient be allergic to the drug or any of the excipients?**
- **Are any of the excipients contraindicated in the patient?**

Pharmaceutical Compounding – Nonsterile Preparations <795>

Patient counseling
- Proper use
- Storage
- Evidence of instability

right

wrong

Patient Counseling

- **Wash hands**
- **Remove wrapper**
- **Lubricate with K-Y Gel or water**
- **Lie on side with lower leg straight and lift buttock to expose rectal area**
- **Using gentle pressure, insert suppository about an inch into the rectum.**
- **Keep still about 15 minutes**
- **Wash hands**

The patient also should be advised:
-To store the supp. in the refrigerator
-To moisten the supp. before insertion with water if it is made of glycerinated gelatin or PEG bases