

Drug Administration through feeding tubes: Tales for the Plumber's Helper

Preparing medication for feeding tubes

Aug 16, 2023



Memorial Sloan Kettering
Cancer Center

Learning Objectives

The participant will be familiar with the key issues in selecting drugs appropriate for feeding tube administration.

The participant will be familiar with drug-nutrient interactions that occur when a drug is co-administered with nutrients through a feeding tube.

The participant will be familiar with controversies and myths regarding withholding nutrition to avoid feeding tube, drug-nutrient interactions.

The participant will be familiar with methods to compound medications appropriately for both gastric and jejunal access feeding tubes

Evaluating the feeding tube patient

Feeding tubes placed through the nose are generally temporary.

- Mostly with distal site in stomach: NGT
- Thinner bore, higher incidence of clogging

Feeding tubes placed through gut wall require surgery, or endoscopic procedure

- These tube are generally shorter, and can be placed into jejunum, PEG, PEJ
- Larger bore, lower incidence of clogging

Less frequent

- Gastric-jejunal tube, gastric site for venting, jejunal site for feeding: GJT
- Oral-gastric, access through mouth, distal site in stomach: OG

Sharing the feeding tube

Since nutrition must share



Intact protein formulas

- Consist of mostly caseinate salts, In most products Ensure, Osmolite
- Will react with acidic medications to form clogs, Low osmolarity

Polymeric formulas

- Consist of whey protein, Peptide based, for patients with poor digestion. Peptamen
- Will react lea with acidic drugs, Higher osmolarity

Elemental Formula

- Just amino acids, Developed by NASA
- Does not react with acidic drugs, no binding with drugs, High osmolarity
- Advised for jejunal administration, but may not be tolerated

Developing Guidance for Feeding Tube Administration of Oral Medications

- Klang MG. Developing guidance for feeding tube administration of oral medications. J Parenteral and Enteral Nutrition. 2023;1-22. doi:10.1002/jpen.2490
- Recently published Podcast:
 - <https://soundcloud.com/user-67457490/developing-guidance-for-feeding-tube-administration-of-oral-medications-jpen>

Pharmaceutical Issues:

Crushing Extended-Release Drug Products

- Destroys Extended-Release properties
- **Increased risk of side effects and toxicities**

Example: Pentoxifylline (Trental) Tablets

	<u>Intact Tab</u>	<u>Crushed Tab</u>
C_{max} :	184 ng/mL	1789 mg/mL
t_{max} :	2.25 hr	0.6 hr
S.E.:	none	Nausea, dizziness, vomiting

- But a suspension can be made – just administer more frequently to avoid side effects

Administering the Drug: ASPEN

Do not add medication to an EN formula

Administer each medication separately

Avoid mixing together different meds given risks

Use liquid dosage forms only if appropriate

Prepare approved immediate-release solid dosage forms as instructed

Use appropriate instruments to prepare or measure enteral medication

Clogged Feeding Tube?

Should be a rare event

Assuming proper care

Can become clogged with

- EN formula
and/or
- Drug residue



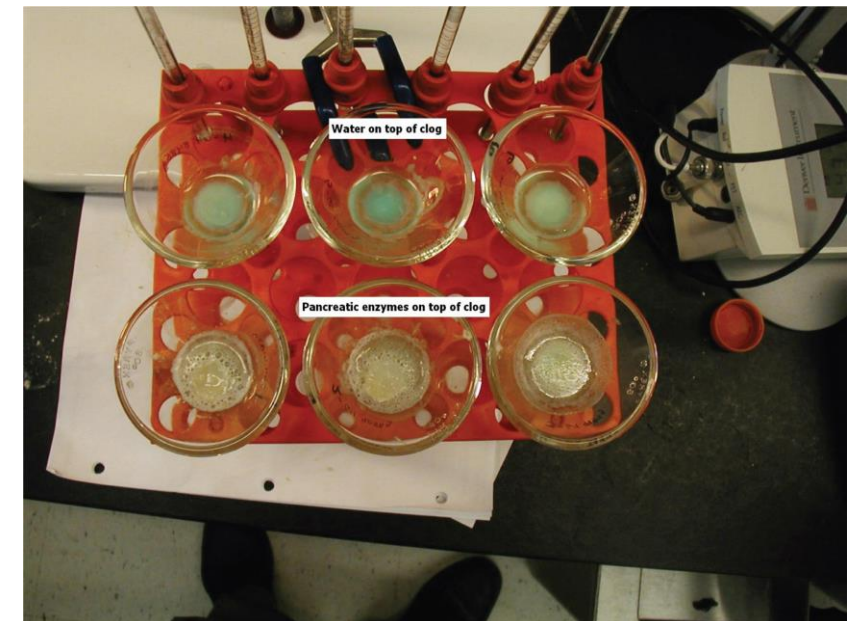
Question: “In your experience, which medications have caused enteral feeding catheter obstruction?”

	<u>% of Responders</u>
Sucralfate (Carafate)	31.3%
Potassium Chloride tablets	27.9%
Theophylline tabs/caps	12.3%
Fiber (Metamucil)	12.3
Phenytoin Tab	11%
Enteric coated medications	10.4%
Miscellaneous	29.2%

Clogs

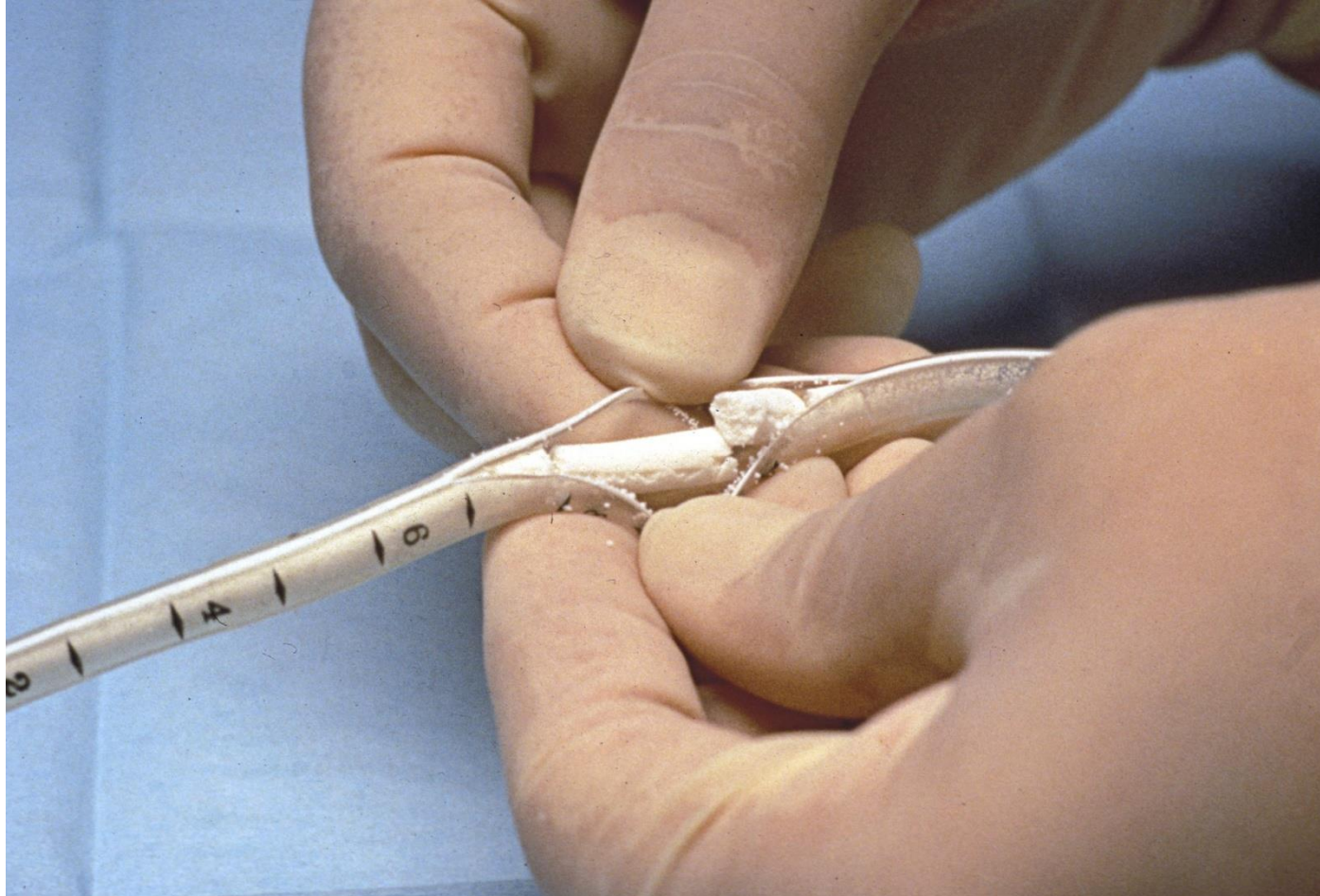
Know the nature of the clog

- If the clog is a drug:
 - Drugs are mostly weak bases and will dissolve with acidic fluids
- Proteins will clog with acidic fluids. (Cutie/Altman)
 - Juices, soda are acidic, but sticky
- Enteric coated enzymes clog
 - Remove coating with Bicarb (45 min @37°C)
- Pharmacy QA incident
 - Pt got enteric drug – clogged tube
- Tube-Clear, fast
- Water worked best



Arriola TA, Hatashima A, Klang MG. Evaluation of extended-release pancreatic enzyme to dissolve a clog. Nutr Clin Pract. Oct 2010;25(5):563-564.

Clogged Feeding tube



- There have been reports of solid tablets clogging tube
- Dr Harvey has a slide with a pink fragment with letters AR

Pancreatic Enzyme to unclog tube

- Viokace is only FDA approved pancreatic enzyme not EC.
- Crush the drug with 5 mL Na Bicarbonate 8.4%
- Will only dissolve protein-based clog
- There is a gummy center
- May make clog worse
- Creon was used in 1 study, but EC
 - Takes > 30 min to remove EC
 - Don't use Creon



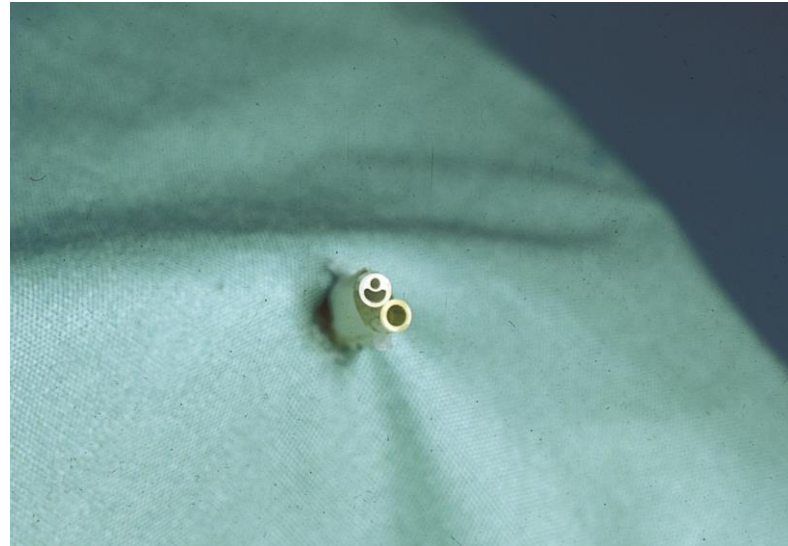
Internal Diameter

Flow through the tube and susceptibility to clogging.

Plays important role in types of formula & medications that can be infused.

Internal diameter can change depending on the device material and model.

- Polyurethane: thinner walls, less comfortable
- Silicone: thicker walls, less stiff



Feeding tube clog issues

More likely to clog

- Longer tubes- especially NJT
- Rate of enteral administration
 - <50 mL/hr for gastric tube get retrograde clogging

Checking for gastric residuals

Using Foley catheters as feeding tube substitute

Less likely to clog

- Short tubes- especially PEG
- Rate of enteral administration
 - Bolus feeding has less clogs and better tolerance

Rinsing reduces clogs

Use tubes with hydromer coating

Relizorb – pancreatic enzyme in-line delivery cartridge (in theory)

Review Drug Delivery issues

For a drug to be absorbed, it first must dissolve

- Magnesium Oxide has high magnesium content
- Worthless as it does not dissolve

Many drugs have poor dissolution and poor rate of absorption.

- Excipients are added to enhance dissolution
- Excipients often are insoluble in water e.g. cellulose

While a liquid formulation might seem ideal for a feeding tube, No liquids are designed for feeding tube administration.

- Liquid meds are for pediatrics – thick and sweet.
- Dissolution ↓ as viscosity ↑

Rock in water – does it dissolve?

Many Pharmaceuticals are insoluble in water

What do we do to improve dissolution?

Heat the lake

add energy

Add more water

Reduce concentration

Increase surface area

Grind to small particle

Poorly soluble drugs

Does the rock dissolve ?

Oral Absorption enhancers – FT implications

Look at ingredients

↑Surface Area

Co-Precipitates

Self Emulsifiers

Enteric coating

PEG matrix

Cyclodextrin

Cellulose – more water

Temporary solubility

Requires contact with low pH

Reduces gastric degrade

Doesn't dissolve

Avoid alcohol containing diluents

Itsy bitsy pieces

To improve dissolution – crush thoroughly
Smaller particle, increased surface area
Adding more fluid reduces clogs.



Why doesn't it dissolve?

Solid Drugs don't dissolve when combine with nutrition

- Reaction with nutrition thickens, reduced dissolution

Suspensions are thick, add water to thin

To improve dissolution, add more water

Surfactants use caution:

- DSS (Colace) will allow mineral oil to be absorbed
- Dangerous, as mineral oil will accumulate in lungs

Crushing Tablets

- Sustained vs immediate release
 - Frequency of dosing
- Scored - If it can be cut – Sometimes -it can be crushed (not for Toprol XL and others)
- Chewable tablets crush coarsely
- Coatings form gummy solids – especially multiple tablets combined
- Shards form from coated tablets: Lipitor



Rinsing the tube

Use water or juice?

- Drug beads are sometimes enteric coated
 - Not Emend (Aprepitant)
 - Not Itraconazole
 - These are drug sprayed onto delivery system
- EC beads are resistant to acid – mix with water and will clump
- Mix with acidic juice – will not clump.
 - Juice is not for jejunal- use water
- Good for stomach – not for lower GI tract

Fun with Chemistry

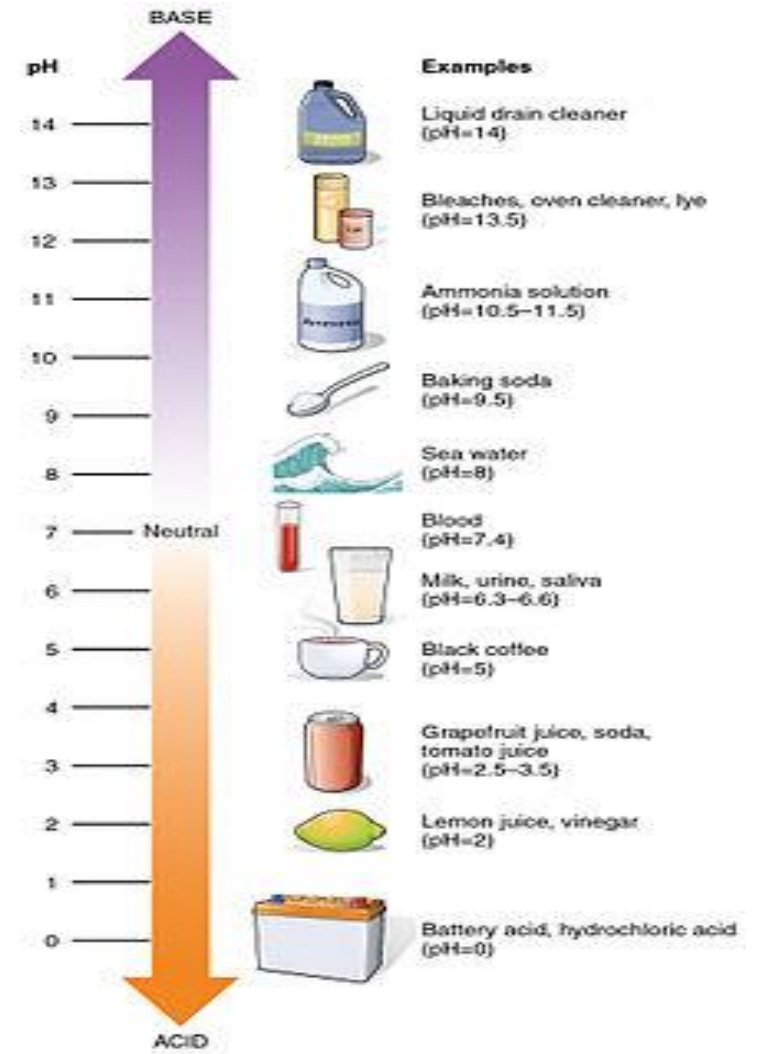
Most Pharmaceutical liquids are acidic

- React with nutrition (Cutie/Altman)

Drug clogs require acidic fluid to dissolve

The jejunum is more basic than stomach.

- Drugs must be dissolved first for absorption
- Solid drug will not dissolve in jejunum as there is little fluid



Food for thought

Intact protein – will react with acids to form clogs

Blender diet – press through cheesecloth to avoid clogs – leave out the walnuts/raisins

Fats congeal – dissolve with ethanol

- Fat reacts with salt to form soaps
- Oils react with Ca and Mg to form

Ethanol is a lubricant and dissolves lipid, soaps and poly-urethane tubes

Elemental diet – individual amino acids – require mixing, stink and have high osmolarity



FT Administration Perspectives

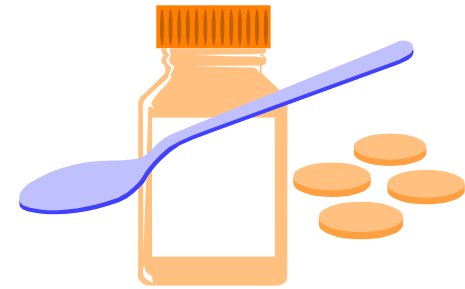
Plain Tablets: Crush & Flush

- Some have coated shells which do not crush well - clog
- Some drugs are poor water solubility and may fall out of solution when mixed with water – mix in syringe
- Some require extra water volume (10-15 ml)
 - Acyclovir, Metformin, Mesna

Hard powder-filled Capsules: Open, Mix, & Flush.

Soft Gelatin Capsules : Create pinhole and extract into syringe or squeeze into feeding tube. (may adhere to tube) – Nifedipine

- Does not work for liquid filled capsules where the contents are thick



Preparing the Drug

Recommendation from ASPEN

Ideally, trained pharmacy personnel are responsible to prepare medication requiring significant manipulation

Use only immediate-release dosage forms

Solid or liquid oral dosage forms only

Use *purified* water source for dilutions (not sterile)

Post-Pyloric Administration



Reduce aspiration?

- Allow gastric rest

Sensitive to osmolality

- Dilute liquid medications

Smaller tubes used

Bypass Stomach

- Binders do not release drug
- Require acid exposure to activate release

PPI's and feeding tubes (Lansoprazole, Omeprazole)

Pick one:

- Open capsule, mix with juice, rinse well 60 ml - gastric
- Mix capsule with sodium bicarbonate – gastric/jejunum
- Use Orally Disintegrating Tablet (ODT) – mix with water 5-15 ml –gastric only
 - Teva version forms clogs

Avoid

- ODT to get “under-the-tongue” absorption Needs an intact GI tract to get drug to site of absorption
- Mixing oral capsule content with water – mixes better with acidic juice (apple juice is best)

Osmotic Issues

Common Side Effects associated with Enteral Nutrition?

- Edes: 40% of TF Diarrhea caused by excipients
Diarrhea, Nausea, Vomiting, Cramping,
Distention & Bloating

Is it caused by:

- The **Enteral Nutrition** ??
- The **Drug Therapy** ??
- Both ??



Osmotic Issues

Inadequate dilution of electrolytes

- 60 mEq KCl requires 6-8 oz of water per 20 mEq

Sorbitol –GRAS- More potent than Lactulose

- Causes diarrhea, amount present unknown

Most Pharmacy-made liquids have high sorbitol

- Many have osmolarities > 1000 mOsm/L
- GI tract tolerates 600 mOsm/L
- Jejunum is acutely sensitive – no diluting capacity

Generic liquid diphenoxylate (Lomotil) – contains sorbitol – oops!

Extemporaneous Compounding

Suspending agents – OraSweet (3240 mOsm 5% Sorbitol

- OraPlus – 230 mOsm - methylcellulose

Some oral formulation will not get absorbed when mixed into a liquid

- e.g., Itraconazole compounded suspension – Stable but not absorbed
- SyrSpend SF – low osmolar suspending agent
 - SyrSpend Alka, higher pH but not longer stability

New 795 issues in compounding liquids

- NEW USP 795, compounded suspensions must be tested for preservatives effectiveness. USP 51
 - And USP 62 Bioburden
 - Also need B&F validation for microbiology tests
- Stability-indicating assay required to establish BUD
 - Few references cite this type of analysis.
 - Potency tests are not acceptable
 - All my HPLC studies meet this criteria
- My personal recommendation: Do not compound a liquid.
 - Do all preparations as extemporaneously compounded.

Osmolality, pH, and Compatibility of Selected Oral Liquid Medications With an Enteral Nutrition Product – JPEN 2012

Evaluated liquid medications

- Checked pH, measured Osmolality
- Mixed 1:1 with Ensure

Checked for visual compatibility

- Generally, acidic drugs form clumps
 - FeSO₄ elixir formed concrete
- Some liquids formed soaps
- Base + Ca = chalk

High osmolar issues

- Ora-sweet - >3000 mOsm/kg
- Cherry Syrup ~ 6165 mOsm/kg
- Syr-Spend ~ 285 mOsm/kg

If liquid is thick, and high reactivity

- Easier to crush tablet and mix with water
- e.g. Furosemide, calcium salts, acyclovir



Drug	pH	Osmolality	I/C
Acetaminophen Solution	4.4	4035	I
Acetaminophen Susp.	4.7	6425	I
Acyclovir Oral Suspension	5.8	4205	I
Aluminum Hydroxide Gel	7.2	1501	C
Al(OH) ₃ , Mg(OH) ₂ , Simeth	7.8	990	C
Aminocaproic Acid Sol	6.2	3405	C
Atovaquone Suspension	5.9	135	I
Azithromycin Suspension	9.5	3950	I
Calcitriol Solution	7.8	NA	I
Calcium Carbonate Susp	9.2	2490	C
Carbamazepine Susp	3.7	4225	I
Cherry Syrup	2.8	6165	I
Dexamethasone Intensol	3.9	10600	I
Digoxin Solution	6.5	5950	C

Klang M, Ng N and McLymont V.
Osmolality, pH and Compatibility of
Selected Oral Liquid Medications with an
Enteral Nutrition Product, *JPEN J Parenter
Enteral Nutr* September 2013 37: 689-694

Holding Tube Feeding

- Major reason patients do not get goal nutrition is holding for drug administration
- Numerous reports – advise to improve absorption
 - Certification exams, textbooks articles
- Much is based on misconceptions of drug interaction and absorption
- Protein Binding
 - Many drugs bind to protein, but no change in absorption
- Drugs include:
 - Sinemet, Dilantin, Levofloxacin, Ciprofloxacin, Synthroid, Warfarin, Tegretol

Impaired Phenytoin Absorption by Enteral Feeding

First described in neurosurgical patients at Harborview Medical Center, University of Washington, Seattle

Patients receiving **continuing nasogastric feeding** failed to absorb standard doses of phenytoin. → EN impairs drug absorption

Patients already stable on phenytoin had a 4-fold reduction in serum phenytoin concentration once NG feeding was started

Early Reports

Cutie/Altman showed in-vitro congealing when formula and suspension mixed

Bauer noted stable patients, become erratic levels

- Assumed drug bound to protein in formula
- Held nutrition and increased dose, but levels were still poor

Bauer Discussion

This drug is strongly protein bound.

- The bound drug bypasses site of absorption

BUT, if drug binds to Nutrition, doesn't Nutrition get absorbed?

His reply, patients get fed liquid nutrition

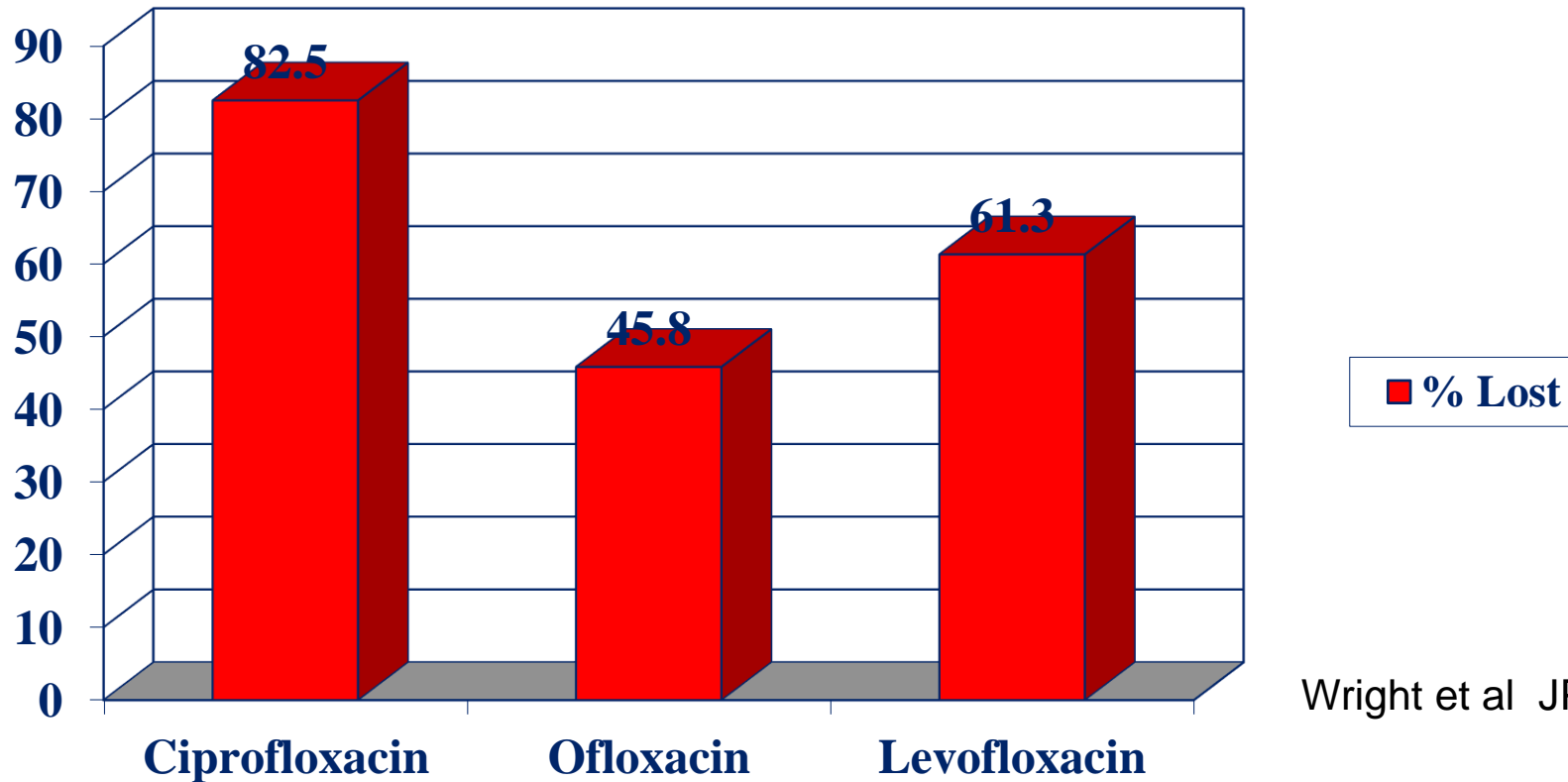
- Liquid in = Liquid out
- Maybe, if you have fast transit time – but not all patients have diarrhea
- Edes showed 40% of Diarrhea caused by high osmolarity of liquid medication.
- Could fast transit result in poor absorption?

Phenytoin Literature review

The most comprehensive review, Au Yeung – Ensom, Ann Pharmcot, 2000

- 29 reports (10 case reports, 4 RCT, 7 in-vitro)
- No interaction seen in 3 RCT (used capsule orally), only found in case reports
- 14 different mechanisms
- Despite failed effects of holding TF, the authors advised this as a remedy

Median % Drug Lost in Ensure compared with H2O



Wright et al JPEN Jan-Feb 2000 24: 42

Withholding nutrition for administration of Phenytoin

Hold the Nutrition

- 1.) Numerous clinical case reports document very low levels when co-administered with tube feeding
- 2.) Drug has poor solubility and slow transit. (BSC Class IV) prone to DNI and binds to protein
- 3.) Numerous recommendations cite hold nutrition as a function of gastric emptying

Do Hold Nutrition

- 1.) Randomized clinical trials show no food interaction with Phenytoin. Only with suspension, not with tablet, injection or capsule.
- 2.) Protein gets absorbed – doesn't leave drug behind
- 3.) Dilution improves amount dissolved - this remedy has never been proven in clinical trial

Withholding nutrition for administration of Warfarin

Hold the Nutrition

- 1.) In vitro analysis showed strong protein binding to nutrition
- 2.) Clinical trial showed improved INR when holding nutrition for 1 hour
- 3.) Numerous recommendations cite hold nutrition.

Do Hold Nutrition

- 1.) Binding study was conducted at pH 8. At acidic pH Warfarin binds to plastic. As pH increases drug falls off.
- 2.) Trial was done in 6 patients with 3 formulas at different rates, fiber, protein, Vitamin K content and rates of administration
- 3.) Avoid Warfarin FT, binds to plastic, falls off and gives bolus. Use a DOAC, or LMW-Heparin

Warfarin: Evangelia Davanos, PharmD, BCNSP, CNSC

Levodopa Studies Review Panel Consensus recommendations

Temporally separate the administration of protein from the administration of levodopa/carbidopa preparations (protein shifting).

Review the nutrition needs of each patient and if the patient requires levodopa/carbidopa, consider EN with a goal at the lower end of their protein needs and advance as tolerated (eg. 0.8 g/kg if not septic or otherwise having an increased need for protein).

Review individual patients and when appropriate increase the dose of levodopa/carbidopa and other anti-Parkinson's medications to achieve appropriate therapeutic results.

Levothyroxine Studies Literature-Based Recommendations

1. Serial monitoring of TFT's weekly until a pharmacokinetic-pharmacodynamic steady state is achieved.
2. Increase levothyroxine by no more than 25mcg/day to achieve euthyroid with continuous enteral feeds.
3. Levothyroxine malabsorption may not be sufficiently avoided by holding EN before and after dose administration.

Levothyroxine Studies Review Panel Consensus recommendations

During initiation or alteration of enteral nutrition therapy, consider increasing the frequency of monitoring TFT's levels to weekly.

Clinically review individual patients and when appropriate increase the dose of levothyroxine to achieve appropriate therapeutic results.

Limited data to support/dispute the practice of holding enteral nutrition before/after administration of a fluoroquinolone to improve drug absorption

Consider changing fluoroquinolone route of delivery such as administering intravenously (IV) rather than crushed tablets

Use an agent in the same class with better bioavailability and once daily drug dosing, such as levofloxacin

Chelation between fluoroquinolone and cations revealed no significant changes in fluoroquinolone concentration

Insufficient evidence to recommend the use of higher doses of a fluoroquinolone with enteral nutrition

Amiodarone NGT not equivalent to PO

- ❖ According to a study (8 NGT vs 120 controls)
- ❖ 3-fold increase in dosage required when NGT
- ❖ Drug has long half-life (58 days)
- ❖ Toxic accumulation toxicity possible
- ❖ Reluctant to recommend triple dose for FT.
- ❖ Drug may be binding to the plastic
- ❖ Really bad study – but is in literature

Kotake T, Takada M, Goto T, Komamura K, Kamakura S, Morishita H. Serum amiodarone and desethylamiodarone concentrations following nasogastric versus oral administration. *J Clin Pharm Ther.* 2006;31(3):237-243.

En-Fit Issues

Set size opening

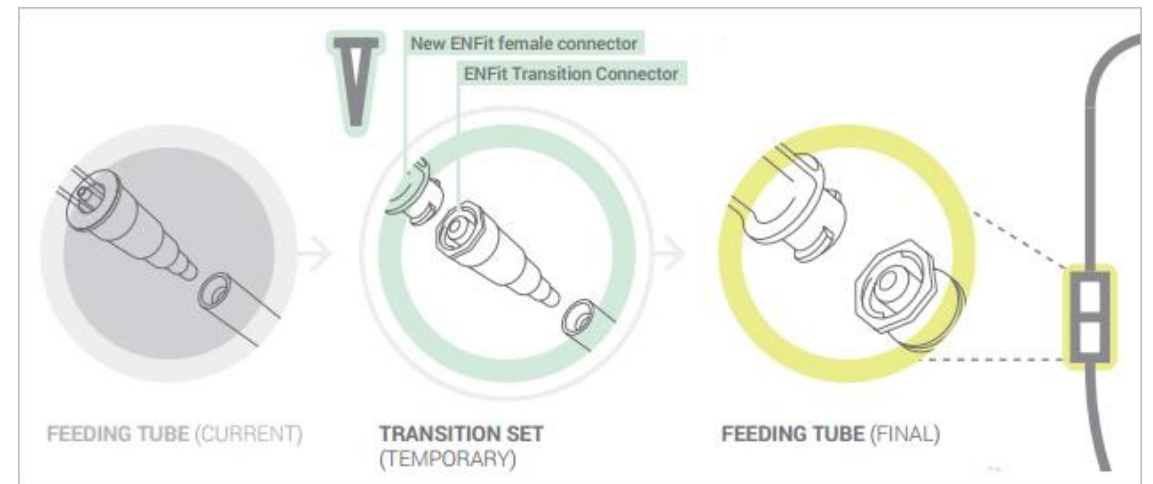
Not ideal for drainage, Blenderized diets and crushed drugs

Port size equivalent to 19 French

No matter how large or small tube diameter
– same size port

Connections get contaminated

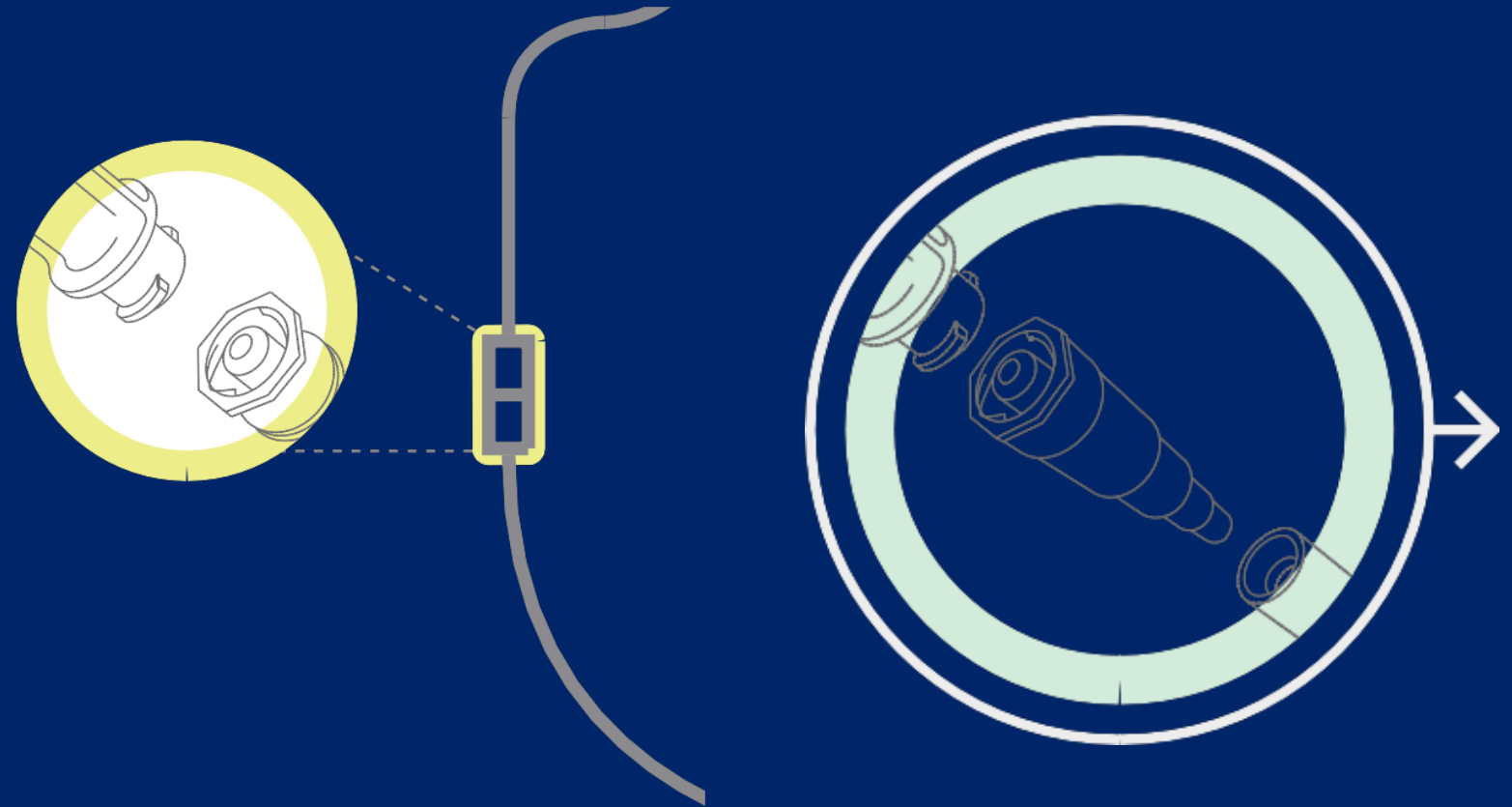
Syringes, bottle caps drip



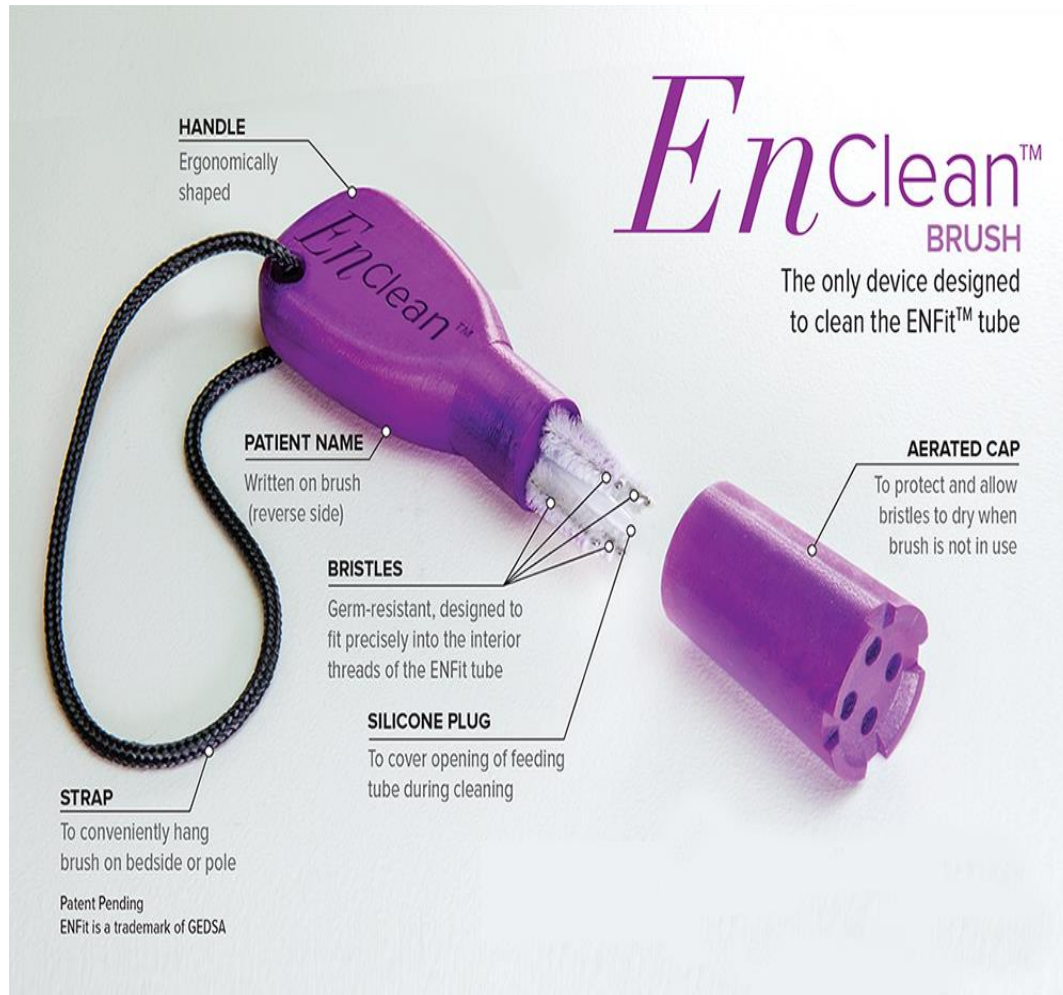
Stay Connected 2014-....?

New **ENFit** connector for all feeding tubes will be introduced this year. Special adapters will be available for first year, but must be phased out

Already available in much of Europe and California



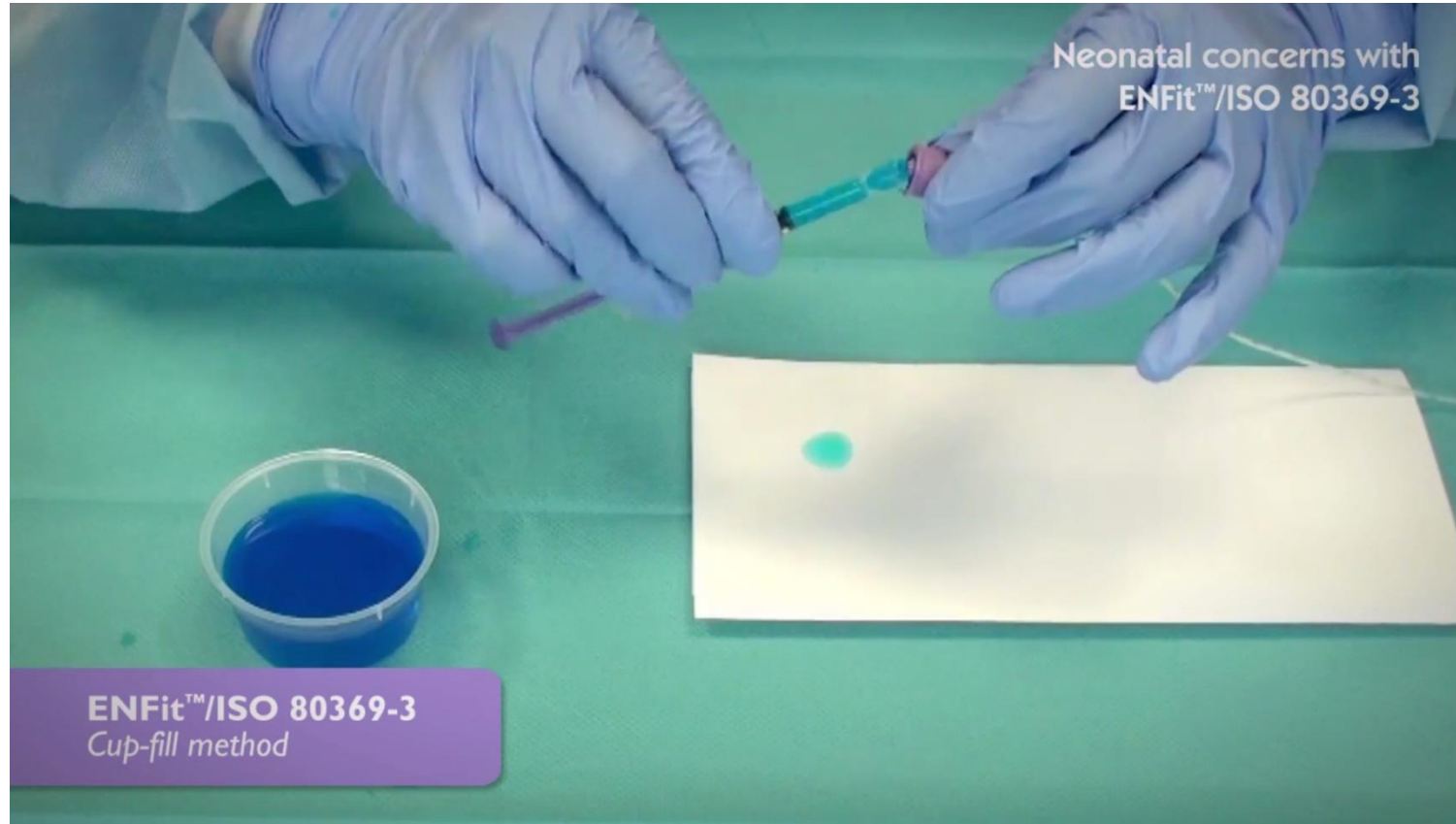
Dirty connections



The female end will accumulate drips from medication, nutrition. May become a source of contamination. Requires frequent cleaning

Recently a study documented the effectiveness of using a toothbrush

EnFit connections leak



**In a YouTube video under ideal conditions attaching the syringe to a feeding tube resulted in a drip
Drips are source of contamination, or drug exposure.**

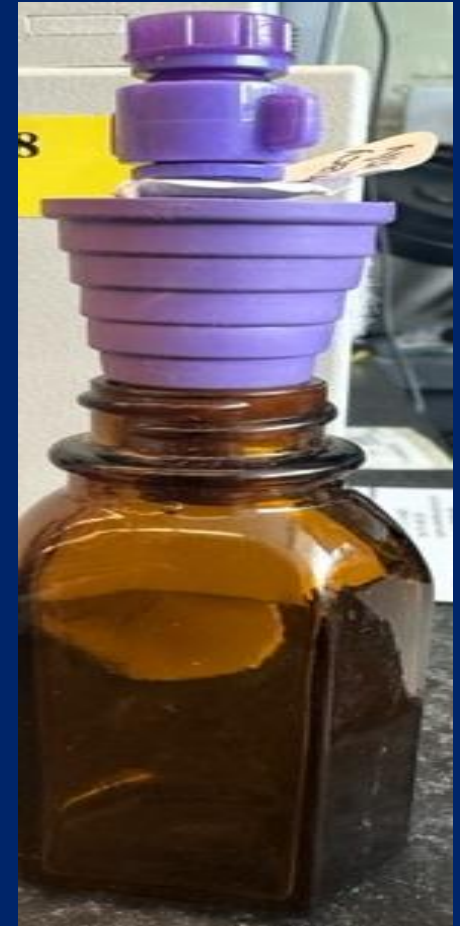
En-Fit Connection Issues

Rigid bottle connector does not allow seal

The soft version does not leak

Errors in measuring

- Air bubble occurs



Hazardous drug

Do not crush oral Chemotherapy

- USP 800 – use N95 mask

Add drug to syringe and allow to dissolve in 15-30 ml Water.

Capsules don't dissolve

- Use Injection
- Etoposide, Cytosin



Chemotherapy administration through FT

It is important that oral chemotherapy which is manipulated, crushed or compounded be afforded the same precautions as does the injectable formulations (OSHA, NIOSH, USP <800>)

Do not open capsules, or crush tablets.

- Use the vented hood and place the tablet / capsule intact inside an oral 30 mL syringe.
- Pull into the syringe 15 ml sterile water for irrigation. Wait 20 minutes for contents to dissolve/ disintegrate.
- Many chemotherapy medications do not dissolve readily.
- The chemotherapy dosage forms which do not disintegrate should not be given by the feeding tube route.

Attach Cap Tip to syringe, Let sit until dissolved- rotate syringe if needed

Syringe Disintegration Procedure

1. Remove plunger from ENFit[®] Syringe Drop required tablets/capsules to prepare single dose in barrel
2. Put plunger back and push to expel air from syringe Withdraw the amount of sterile water as directed on the ORAL CHEMO COMPOUNDING TABLE into syringe from a sterile water irrigation bottle



Crushing Disintegration Procedure

1. Place tablets/capsules into Rx Crush™ ENFit® Pill Pouch and seal.
2. Fill ENFit® 60 ml syringe with required amount of clean water.
3. Connect water filled syringe to nozzle on ENFit® pill pouch. Do not inject water yet.
4. Position pill pouch zip seal under Rx Crush™ roller. Roll over the zip seal to ensure closure.
5. Hold syringe to the side and use the crush plate to crush pills by moving handle up and down. Nibbling at the pills is effective at breaking large or hard pills, or many pills at once.



Recommendations

Liquid Drug forms preferred

- If hypertonic, viscous, thick dilute w/50-60mL water (3 times the volume)

Do NOT crush sustained-release drugs

Mix tablets / hard gelatin capsules with
10-15mL water

Most clogs are drugs

Recommendations (cont.)

Do not add drugs to container or formula

Continuous feeding stopped (0-30min.) and tube flushed with 15-30mL water

Administer each dose separately and flush with 3-5mL between doses

Flush tube with 15-30mL water after last dose

Learning Assessment Questions

Which of the following medications should not be administered into a PEJ?

- 1.) Levofloxacin
- 2.) Warfarin
- 3.) Levothyroxine
- 4.) Sucralfate

References

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