Nutritional Therapy for Cystic Fibrosis

- Dietary counseling to achieve high calorie high protein diet
- Optimize enzyme therapy
- Optimize fat soluble vitamin therapy
- Dietary counseling to achieve adequate salt intake
- Recommendations for supplements/GT placement when appropriate
- Management of CFRD
Pancreatic Enzyme Replacement Therapy (PERT)

- Implemented in adults and children who are pancreatic insufficient
- Approximately 85-90% of patients with CF
Process of Digestion and Absorption
Assessment of Pancreatic Function

- Secretin-pancreozymin stimulation test
- Immunoreactive trypsinogen
- Stool chymotrypsin
- **Stool elastase**
- 72 hour coefficient of fat absorption
Stool Elastase

- An indirect measure of pancreatic function
- Pancreatic elastase is a human and pancreas specific enzyme measured in the stool
- Reflects the levels of other pancreatic enzymes
- Elastase values of 200 ug/g or greater indicates pancreatic sufficiency
- Elastase values less than 15 ug/g reflective of severe pancreatic insufficiency
Pancreatic Enzymes

- Enteric coated microspheres
- Resist inactivation by gastric acid
- Failed pancreatic bicarbonate secretion results in delayed activation
- Strength of enzymes expressed in lipase units
- Dose based on weight and fat content of meal
- High doses may result in fibrosing colonopathy
Factors that Influence Individual Response to PERT

- Variation in enzyme content
- Duodenal pH
- Storage
- Grazing behavior
- Poor adherence (treatment burden, desire to be thin, etc)
Discussion Point: How can I help my enzymes do their job?

- Take enzymes right before and/or during meals and snacks
- Discard enzymes that are beyond their expiration date
- Store enzymes in a cool dry place
- Take with EVERYTHING EXCEPT: foods that contain simple sugars such as hard candy, fruit, fruit juice, jello, soda
For Younger Children…

- Do not sprinkle enzyme beads on food and let sit
- Give enzyme beads in the first bite or two in an acidic food (such as applesauce, other fruit purees, jelly, ketchup)
- Avoid grazing/snacking all day long
- Avoid excess juice
- Don’t forget enzymes with milk/supplements that are consumed alone
Discussion Point: How do I know if my enzymes are working well?

Unhealthy Bowel Movements

- Frequent BMs
- More than 48 hrs without BM
- Loose/diarrhea BM
- Excessive gas/bloating
- Floating/greasy BMs
- Foul odor
- Hard to pass

Healthy Bowel Movements

- 1-2 BM/day
- Sink
- Odor no worse than other family members
- Solid BM
- Brown in color
- No strain or discomfort
Discussion Point: What do I do if I experience any of these symptoms?

- Monitor more closely
- If you see a pattern....

Call your team for advice about adjusting enzyme dose
Discussion Point: Why was my brand of enzymes taken off the market?
History of Enzyme Therapy

- developed enzymes in 1930
- enteric coated microspheres in 1970
- high lipase enzymes required in 1990
- fibroating colonopathy recognized in 2010
- FDA approval required in 2010
Issues with Enzyme Content and Solubility


FDA Guidance for NDA

- Require batch-to-batch consistency
- Require stability at 100% of label claim for lipase
- Safety and efficacy studies required to demonstrate clinical benefit
- Studies must include children
Enzymes in Review

- Creon (Solvay) Received FDA approval 5/09
- Zenpep (Eurand) Received FDA approval 8/09
- Ultrase (Axcan Pharma) under review
- Pancrecarb (Digestive Care) under review
- Pancreaze (Ortho-McNeil) FDA approval 4/10
- Liprotamase (Alnara) under review
An international open-label study of the long-term safety of liprotamase for treatment of pancreatic insufficiency in cystic fibrosis

Drucy Borowitz,* Christopher Stevens,† Candida Frataazzi,† Donna Cohen,† and Marilyn Campion†

- Phase III open-label prospective 1 year international study
- Inclusion criteria: > 7 y.o., Fecal elastase < 100 ug/g
- N= 215 (45 sites: 34 US, 11 outside US)
- Given 1 capsule (32,500 USP units of lipase) in the middle of 3 meals and 2 snacks daily
- Follow up exams at 1-2 week and then 1-2 month intervals for one year
- Looked at vitals, anthropometrics, labs (including fat soluble vitamins)
- 145 completed the full year
- 69 early withdrawal (17% from adverse events; generally GI c/o’s or pulmonary exacerbations)
Conclusions

- Liprotamase treatment was well-tolerated
- Adverse events followed expected patterns for CF
- Stable pulmonary fxn (measured by FEV1)
- Stable ht, wt, BMI, fat soluble vitamin levels, pre-albumin, albumin, cholesterol and TG
- Patients took on average 5.2 capsules per day, less than usual daily dose for most CF patients (average 20 capsules per day)
Enzymes Currently FDA Approved

- **Creon** (Solvay 6,000/12,000/24,000 USP Lipase)
- **Zenpep** (Eurand 5,000/10,000/15,000/20,000 USP Lipase)
- **Pancreaze** (Ortho-McNeil 4,200/10,500/16,800/21,000 USP Lipase)
- **Pancrelipase** (X-Gen 5,000 USP Lipase)

*authorized generic enzyme for Zenpep*
Summary

- Enzyme therapy is an important part of nutritional management in cystic fibrosis
- There are steps you can take to improve response to enzyme therapy
- Due to concerns with product stability and variability, enzyme manufacturers are now required to obtain FDA approval prior to marketing