THE WORLD OF CYSTIC FIBROSIS
GASTRO INTESTINAL AND NUTRITIONAL CHALLENGES

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Objectives
- The CFTR gene mutation, Pathogenesis
- Recent advances in diagnosis and treatment
- Gastrointestinal Manifestations
- Nutritional Challenges and Complications
- Treatment, nutritional rehabilitation, and controversies

Sixty Five Roses!
- Mucoviscidosis
- Transmembrane Conductance Regulator, CFTR
- Dr. Dorothy Hansine Andersen

Professor Monty Losowsky
Harry Shwachman
Dr. Paul di Sant'Agnese
Dr. John Mangos
Dr. Jean Feigelson
Dr. Charlotte Anderson
Professor Mary Ellen Avery
Professor Flensborg


Why the lungs and pancreas?!

- Respiratory tract
- Sinusitis
- Nasal Polyps
- Pancreatic exocrine
- CF related Diabetes
- Gastrointestinal
- Hepatobiliary
- Sweat glands
- Exocrine tissues
- Reproductive system
- Coagulation defect

Molecular Consequences of CFTR Mutations

- CFTR Courtesy of the NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health
- Courtesy of Carol D. Guzé, Ph.D. Medical Geneticist, ABMG, - Human Genetics

Pathophysiology Molecular Consequences of CFTR Mutations

- Courtesy of Carol D. Guzé, Ph.D. Medical Geneticist, ABMG, - Human Genetics
Pathophysiology Molecular Consequences of CFTR Mutations

<table>
<thead>
<tr>
<th>Defect</th>
<th>Classification</th>
<th>Normal</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
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<tr>
<td>Molecular</td>
<td>Dysfunction</td>
<td>No change</td>
<td>Block in Focusing</td>
<td>Block in Regulation</td>
<td>Altered Conduction</td>
<td>Reduced Synthesis</td>
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<td>Type of Mutation</td>
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<td>Missense</td>
<td>Missense</td>
<td>Missense</td>
<td>Missense</td>
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LIMITATIONS
- False negative if complete pancreatic fibrosis
- Meconium ileus
- Pancreatic sufficient CF
- Heterozygous carriers
- Degree of elevation does not correlate with severity

Immunoreactive trypsinogen

Meconium Ileus

A Progressive Pancreatic disease

LIMITATIONS
- Shelf Life
- Storage temperature
- FDA approval
- Accuracy of dosage
- Efficacy pH dependent
- Timing with meals
- Adequacy to amount of fat ingested
- Porcine protein allergy
- Religious beliefs
- Oral ulcers – no longer a challenge

Pancreatic Enzyme Replacement Therapy

Fibrosing Colonopathy
Courtesy of the Children's Hospital of Philadelphia, PA.


Hepatobiliary Abnormalities

- Hepatic Steatosis
- Biliary Cirrhosis
- Portal Hypertension
- Esophageal varices
- Chronic liver disease
- CBD stricture
- Cholelithiasis

Hepatic steatosis

Courtesy of Eduardo Rucelli, MD, Children's Hospital of Philadelphia, PA.
Hepatobiliary Abnormalities

- Portal Hypertension
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Hepatobiliary Abnormalities

CF related Liver Disease

- TPN related cholestasis
- Line sepsis
- Hepatotoxic medications

Malignancy

- Risk of malignancy
- Carcinomas of the digestive tract
- Cancers of the esophagus, stomach, small bowel, colon, liver, biliary tract, pancreas, and rectum
- Differential localization and expression of the cystic fibrosis transmembrane regulator gene
- Ancillary effects of CF
- Barrett esophagus
- Gallstones
- Gut epithelial cell turnover
- Antioxidant deficiencies
Nutritional Challenges

- ↑ caloric expenditure in CF exacerbation
- ↑ metabolic rate
- ↑ nutritional requirements
- ↑ gastrointestinal losses
- Chronic diarrhea in short bowel secondary to SBS
- Small bowel bacterial overgrowth
- GERD
- ↓ oral intake
- ↓ intestinal absorption in pancreatic insufficiency
- ↓ / Dysmotility
- DIOS
- Chronic constipation
- ↓ Oral motor skills – mastication
- Oral aversion

Distal Intestinal Obstruction Syndrome

Nutrition

Short Bowel Syndrome

- Location
- Extent
- Functionality
- Viscid mucus
- Gastric hypersecretion
- Malabsorption

Small Bowel Bacterial Overgrowth

- Structural abnormalities, SBS
- Decreased gastric acidity
- Decreased peristaltic activity
- Mucosal damage or atrophy
- Bowel mucosal integrity and mucin
- Impaired immunity, Igs
- Malabsorption of bile acids, fats, carbohydrates, proteins, vitamins
- Damage to the lining of the luminal surface by bacteria
- Transformation of nutrients into toxic metabolites

DIOS
- Decreased function of the enterocytes
- Subsequent malabsorption
- Secretory diarrhea
- Deconjugation of bile acids
- Steatorrhea
- Carbohydrate malabsorption
- CHA fermentation
- Reduced pH
- Osmotic diarrhea
- Colonic mucosa water secretion

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Probiotics

**Probiotics in Small Bowel Bacterial Overgrowth**

Probiotics in Small Bowel Bacterial Overgrowth

Minna K. Salminen, Soile Tynkkynen, Hilpi Rautelin, Maija Saxelin, Martti Vaara, Petri Ruutu, Seppo Sarna, Ville Valtonen, and Asko Järvinen. Lactobacillus Bacteremia during a Rapid Increase in Probiotic Use of Lactobacillus rhamnosus GG in Finland. • Clinical Infectious Diseases 2002; 35:1155–60

Primum non nocere

- Fibrosing Colonopathy
- Proton Pump Inhibitors
- Intestinal Unstirred Water Layer – NAC – PEG 3350
- Hepatic Steatosis
- Probiotics – Line Colonization
- Survival - Quality of Life
- PGD – CVS – Amniocentesis
- Ethics of Termination

Thank You!

Ruba Abdelhadi, M.D.