Cystic Fibrosis
Cystic fibrosis (CF) is caused by a defective gene and its protein which causes the body to produce abnormally thick and sticky mucus.

Basic defect is a faulty chloride transport that causes mucus build up that results in lung dysfunction, pancreatic insufficiency, intestinal diseases, and infertility.
Cystic Fibrosis

- Most common life-threatening genetic disorder in Caucasians
- Autosomal-recesesive disorder with more than 1900 mutations in the CFTR (CF transmembrane conductance regulator) gene
- No identifiable cure is known
CFTR gene codes for a protein called the cystic fibrosis transmembrane conductance regulator

Function of CFTR protein:

- Channel in membrane of cells that produces mucus, sweat, saliva, tears, and digestive enzymes
- Transports chloride into and out of cells; helps control movement of water in tissues for thin mucus production
- Transports sodium ions across cell membranes; important for function of organs
Cystic Fibrosis

- In 1938, 70% of CF babies died within the first year of life.
- Average life expectancy age today is 37 years old.
- The most prevalent CF-causing mutation in the Caucasian population, 86% of CF alleles of cases is the F508del mutation.
F508 mutation

- Mutation in the gene for the CFTR protein. The mutation deletes three nucleotides that code for phenylalanine.
- Causes a person to produce CFTR without phenylalanine
- CFTR protein breaks down because of its abnormality and cannot escape to move to its correct cell location
Prevalence & Incidence

- Approximately 80,000 people in the world are diagnosed with CF. 30,000 of those 80,000 people are in the United States
- 1 in 3500 live births have Cystic Fibrosis
- More than 70% of patients are diagnosed by age two.
- More than 45% of the CF patient population is age 18 or older
Neonatal cystic fibrosis screening
First test: A sample of blood sample is taken from the bottom of the baby's foot or a vein in the arm
The blood sample is examined for increased levels of immunoreactive trypsinogen (IRT), a protein produced by the pancreas that is linked to CF
Gold standard for diagnosis is the sweat chloride test (pilocarpine iontophoresis)

Test used to induce sweating then the sweat electrolytes are measured
For infants up to 6 months of age
- Chloride levels of:
  - Less than 29 mmol/L = CF is very unlikely
  - 30-59 mmol/L = CF is possible
  - Greater than 60 mmol/L = CF to be diagnosed

For people older than 6 months of age
- Chloride levels of:
  - Less than 39 mmol/L = CF is very unlikely
  - 40-59 mmol/L = CF is possible
  - Greater than 60 mmol/L = CF to be diagnosed
Diagnosis

- Other Tests
- Prenatal Screening
  - Genetic testing can show if the fetus has CF
  - Amniocentesis - removing small amounts of fluid from the sac around the baby
  - Tested to see if the CFTR genes are normal
  - Chorionic villus testing - removing a tissue sample from placenta to test for CF
- Chest x ray
- Sinus x-ray
- Lung function tests
- Sputum culture
- Trypsin and chymotrypsin in stool
Quality of Life

- Back pain and headaches in 89% of adults with CF
- Chest pain in 16-64% of CF adults
- Pain can cause anxiety and depression
- Females are observed to have a lower quality of life
Quality of Life

- Sleep disturbances can occur
  - Patients with airflow limitation; have sleep related hypoventilation, hypovolemic and hypoxemia
  - Mucus and gastric reflux can cause nocturnal cough episodes
  - Pain
Congenital bilateral absence of the vas deferens (CBAVD) accounts for 1-2% of male infertility

Men: All men with CF are azoospermia, infertile, and have CBAVD

50% of men with CBAVD carry two or more CFTR mutations

Women can be fertile; controversial to whether or not they should become pregnant
### Sinopulmonary
- Infection
- ABPA
- Sinusitis
- Polyposis
- ABPA
- Haemoptysis, pneumothorax
- Respiratory failure
- Sinusitis, polyposis, anosmia

### Gastrointestinal
- Fetal echogenic bowel
- Meconium ileus
- Pancreatic insufficiency
- Rectal prolapse
- DIOS
- Intussusception
- Hepatic steatosis, biliary fibrosis
- Rectal prolapse
- DIOS
- Intussusception
- Biliary fibrosis, cirrhosis
- Digestive tract cancer (adenocarcinoma)

### Renal, endocrine, other
- Dehydration
- Hyponatraemic hypochloraemic metabolic alkalosis
- Renal calculi
- Hyponatraemic hypochloraemic metabolic alkalosis
- Delayed puberty, osteoporosis, CFRD
- Renal calculi, renal failure
- CBAVD, HPOA
- Arthritis, vasculitis
- Hyponatraemic hypochloraemic metabolic alkalosis

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The chart above outlines different conditions grouped under three categories: Sinopulmonary, Gastrointestinal, and Renal, endocrine, other, with their associated symptoms or disorders.

**Infancy**
- Fetal echogenic bowel
- Meconium ileus
- Pancreatic insufficiency
- Rectal prolapse

**Childhood**
- DIOS
- Intussusception
- Hepatic steatosis, biliary fibrosis
- Rectal prolapse

**Adolescence/adulthood**
- DIOS
- Intussusception
- Biliary fibrosis, cirrhosis
- Digestive tract cancer (adenocarcinoma)
- Delayed puberty, osteoporosis, CFRD
- Renal calculi, renal failure
- CBAVD, HPOA
- Arthritis, vasculitis
- Hyponatraemic hypochloraemic metabolic alkalosis
Cystic Fibrosis
Transmembrane Regulator
- Water follows chloride
- Thick mucus develops
Signs and Symptoms

- Salty sweat
- Frequent Infections (Pneumonia, Bronchitis)
- Nasal polyps
- Cough and sputum production
- Wheezing and air trapping
- Digital clubbing
- Infertility
Nutritional S/S

- Failure to Thrive
- Edema
- (hypoproteinemia)
- Chronic pancreatitis
- Cirrhosis
- Pancreatic exocrine insufficiency
- Steatorrhea
Organs Affected

- Lungs
- Pancreas
- Liver
- Intestines
- Sinuses
- Sex Organs
Airway Surface Liquid
Cilia
Bacteria
Inflammation
Bronchioles in Young Adult with CF:
Infections

- The mucous is so thick that it is typically anaerobic
- Biofilms form easily in this environment
- Neutrophils have poor mobility to fight off infections
Pseudomonas aeruginosa
- Present in 80% of adult patients
- Gradual decrease in lung function
- Poor clinical status
- Drug resistant (antibiotics treatment usually ineffective)
Pancreas

- Pathophysiology
Pathophysiology

Bicarbonate

Volume

pH
Pancreas

- Anatomy

- Gall bladder
- Common bile duct
- Pyloric sphincter
- Pancreas
- Pancreatic duct
- Duodenum
- Acinar cell
- Duct cell
- Alpha cell
- Beta cell
- Delta cell
- Islet of Langerhans
- Pancreatic acini
- Red blood cells
- PP cell

Nature Reviews | Cancer
Lipase excretion must be below 10% before symptoms appear

85% of CF patients require enzyme replacement therapy due to pancreatic insufficiency (PI)
Pancreatic Insufficiency

- Meconium Ileus
- Maldigestion/absorption
  - Failure to Thrive/Growth Retardation
  - Steatorrhea
  - Deficiencies in fat soluble vitamins
Diabetes in CF

- Cystic Fibrosis Related Diabetes (CFRD)
- Affects about 1/3 of adult CF patients
- Due to beta cell degradation
- Frequent OGTT recommended
- As CF longevity increases more microvascular complications are present
Typical diabetic diets are inappropriate
Increased energy needs through a high fat diet, also high starch
Limited treatment is typical because of treatment demands of CF
  • risk noncompliance/overwhelming patient
Insulin is used when necessary
Liver disease is the 3rd cause of death in CF
Fatty liver causes hepatomegaly
Commonly asymptomatic
Focal Biliary Fibrosis
Severe scarring can lead to cirrhosis
Varices, hemorrhaging
Best treatment: Liver transplant
Distal Intestinal Obstructive Syndrome (DIOS)
- Due to thickened fecal matter
- Adult equivalent of maconeum ileus

Rectal Prolapse
Medical Care: Goals

- Preventing and controlling lung infections
- Loosening and removing mucus from the lungs
- Preventing and treating intestinal blockage
- Providing adequate nutrition and absorption
Medications

- Antibiotics
- Mucus thinning drugs
- Bronchodilators
- Oral pancreatic enzymes
- Inflammatory treatment
Physical Therapy

- Postural Drainage and Percussion
  - 4-5 minutes in 2-3 positions, 1-4 times per day
Mechanical Devices

- Mechanical Percussor
Inflatable Vests: high frequency chest wall oscillation
Active Cycle of Breathing

- Breathing control
  - 20/30 seconds
- Huffing followed by cough if needed
- 3-4 deep breaths
- Breathing control
- 3-4 deep breaths
- Breathing control
Breathing Techniques

- Positive Expiratory Pressure
  - Masks increase force required to exhale
Pulmonary Rehabilitation

- Long term program to improve lung function and overall well-being
- Attended weekly
- Includes:
  - Exercise training
  - Nutritional counseling
  - Energy conserving techniques
  - Breathing strategies
  - Psychological counseling or group support or both
  - Education on how to manage disease
Complementary and Alternative Medicine

- In 2008 CAM was used by 75% of patients

- Examples:
  - Garlic Capsules: antibacterial properties
  - Ginseng: antimicrobial
  - Curcumin: Increase CFTR activity

- Only limited evidence of their effectiveness.
Exercise Treatment

- Exercise is always recommended
- Clears the airway and improves lung function
- Helps improve quality of life
- Higher levels of aerobic exercise have been associated with prolonged survival
Exercise Treatment

- Aerobic training is essential to increase VO2 peak (increase survival)
- Benefits from strength training. Anaerobic training can help increase aerobic capacity
- Inspiratory muscle function (IMF) is intense breathing exercises that strengthen the muscles around the lungs
- Without IMF, pulmonary compliance decreases and residual volume increases
Lung Transplants

- Most severe conditions and other treatments are no longer working
- Must be healthy enough for a transplant (only affected by the disease causing the demise of the lung)
- CF is the third most common reason in adults
- CF is the most common reason in children
Tests for lung transplant approval

- Lung function tests
- Blood tests
- Chest CT scan
Lung Transplants

- For most severe cases, when other treatments fail
- High risk procedure:
  - Mortality rates: 5-20%
- 30% suffer from post-surgical complications
- Only way to restore function
- 5 year survival rates:
  - 72% with transplants
  - 33% without transplants
Types of Transplants

- Single-lung transplant is not performed
- Double-lung transplant
  - Usually takes 6-12 hours
- Living donor lobar lung transplant
  - Healthy adult donates a segment, or lobe, of one lung to another person
Lung transplants are last option

Possibility of improving quality of life

Serious Risks
- The recipients’ body may reject the lung
- Infections

Survival Rates
- About 78% of patients survive the first year
- 63% of patients survive 3 years
- 51% of patients survive 5 years
MNT for Cystic Fibrosis

- Goal: control malabsorption, maldigestion, provide adequate nutrients, promote optimal growth or maintain weight, support pulmonary function, and prevent nutrient deficiencies.

* MNT is specific to each patient; coordinated with other treatments, medications, and chest physical therapy.
Types of MNT:

- replacing digestive enzymes
- respiratory therapy
- COX inhibitors to decrease inflammation
- Agents that increase cAMP (like theophylline) to open chloride channels
How to administer MNT:

- Monitor ongoing nutrition status
- Supply pancreatic enzyme replacement therapy (PERT)
- Meet increased energy requirements
- Provide vitamin/mineral supplements
PERT is first step taken to correct maldigestion/malabsorption.

Microspheres are taken orally, designed to withstand the acidic stomach, and release enzymes in the duodenum for digestion of macronutrients.

The degree of pancreatic insufficiency, amount of food eaten, and types of enzymes taken determine the quantity to take.
the enzyme dosage per meal is adjusted to control GI symptoms (steatorrhea) and promote growth.

- monitoring fecal elastase, fecal fat, or nitrogen balance may help evaluate adequate enzyme dosage and efficacy.
- Fecal elastase is the enzyme secreted by the pancreas to digest proteins and is involved in hydrolysis of peptide bonds.
MNT for children

- Evaluate and monitor growth and development (body composition, BMI, wt, ht, head circumference, bone status, etc)
- Identify degree of pancreatic insufficiency
- Determine PERT recommendation
Macronutrient needs

- Energy Intake:
- Based on sex, age, BMR, physical activity, respiratory infection, severity of disease, and severity of malabsorption
- There are equations to calculate energy needs when labs aren't available.
- CF patients shouldn't decrease PA but rather increase energy intake
- For Children: high energy (based on growth needs), moderate to high fat, and complementary PERT
- For Adults: high energy (to maintain weight)
Macronutrient needs

- **CHO needs:**
  - needs change as disease progresses
  - CF patients may develop lactose intolerances

- **Protein needs:**
  - Slightly increased, but 15--20% should meet DRI for protein requirements

- **FAT needs:**
  - CF patients have increased fat needs; 35-40% of total kcals (especially sources of EFA)
  - Check for EFA deficiencies in regular lipid profiles
  - Also watch for fat-soluble vitamin deficiencies since there is likely fat malabsorption.
  - Fat intolerances found in stool samples.
Specific Vitamin Recommendations

- **Water soluble vitamins:**
  - Adequately absorbed; requirements are met by diet and multivitamin/mineral supplement.

- **Fat soluble vitamins:**
  - Usually inadequately absorbed (fat malabsorption)
  - Low serum vitamin A - impaired mobilization and transportation from liver.
  - Decreased vitamin D - related to decreased bone mineral content
  - Low vitamin E - hemolytic anemia and abnormal neurologic findings.
  - Vitamin K deficiency - secondary to antibiotics or liver disease.
Mineral needs

- Intake should meet CF patients gender/age recommendations.
- Minerals to watch:
- Na requirements increase because increased losses in sweat. Deficiency is evident with lethargy, vomiting, and dehydration. Supplemental salt is required only in some conditions (infants b/c low Na content in BM, Formula and baby food, adults and children during fever, hot weather, or exercise)
Minerals to watch (cont)

- **Calcium** - watch for decreased bone mineralization during childhood esp.
- **Iron** - check yearly in children, and monitor hgb and hct
- **Zinc** - decreased absorption and increased zinc in stools (esp in children and infants). Also related to vitamin A levels.
Feeding Strategies -

- MEET THE NUTRIENT REQUIREMENTS
- Infants: PERT by mouth or added to baby food, supplementation of high-calorie formula.
- Children and adults: Regular and enjoyable mealtimes, larger food portions, extra snacks, high-nutrient density, fortified beverages, puddings, etc.

*feeding tube is alternative for patients who can't meet nutrient needs orally.
*TPN is used short term & after GI surgery.
Results can be evidenced in improved weight gain, slowed decline in pulmonary function, decreased respiratory infection, and improved sense of well being and quality of life.
Case Study: LJ

Age: 14
Female
Student
Mother is 41,
grandmother is 66,
half-brother is 5
Caucasian

"I caught a cold, and it has just gotten worse. My regular treatments were not working, and my doctor says I probably have pneumonia."
<table>
<thead>
<tr>
<th>Current anthropometrics:</th>
<th>3 months ago:</th>
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<tbody>
<tr>
<td>Ht: 5'5&quot;</td>
<td>UBW: 110-115 #</td>
</tr>
<tr>
<td>Wt: 102 #</td>
<td></td>
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</tbody>
</table>
Diagnosed with CF at 6 mos.
Since then uneventful disease course.
Hospitalized several times for respiratory infections but otherwise has been maintained by outpatient therapy.
Seen yearly in CF clinic
Uses high-frequency chest compression for 1 hour twice daily
PMH - seen in hospital over year ago.
Very active, runs 3-5 miles 5-6x week.
Meds: Pancreas (1-3 capfuls after meals), Prevacid (20mg daily), Humabid (1/2 tablet every 12 hours), multivitamin and Proventil PRN.

Family Hx: T2DM maternal grandmother, and CF paternal great aunt (deceased)

Nutrition Hx: Not good appetite, Never knows how much Pancrease to take. Likes most foods, but never drinks milk. Likes F/V but doesn't eat many.

“I am not really home for meals that much”

“I take more pancreas if I eat more fat”
AM - rarely eats
Lunch - 3 T crunchy PB or 2 oz ham + 2 oz swiss cheese sandwich, 2-3 oz chips, 1 orange or other fruit, water
Dinner - 5-6 oz of chicken, pork or beef (grilled or baked), 1-2 c raw vegetables on lettuce, 1/4 c ranch dressing, 1 c pasta, potatoes, or rice, usually with 1-2 T margarine, water.

*really depends on whether eats at home or friends'
PES statement for LJ

Inappropriate administration of medication related to repeated infection as evidenced by pneumonia and cold.

Inadequate oral intake related to lack of nutrient absorption as evidenced by weight loss.
Sample diet for LJ

AM - 1 slice toast with margarine, 1 piece of fruit, 1 c milk

Lunch - 2 slices bread, 3-4 oz ham or other lunch meat, 2-3 oz swiss cheese, lettuce, tomato, mayonnaise, mustard (sandwich), 1 piece of fruit, caloric drink

Dinner - 3-4 oz chicken or beef, 1 cup pasta or rice, cream sauce, steamed vegetables with margarine, 1 cup milk.

*avoid "diet" or low fat items, and increase fat intake.


