What is Cystic Fibrosis-Related Diabetes

- Combination of insulin deficiency and insulin resistance
- Average age onset 18-24 years
- 30% of people older than 18 years of age with CF have CFRD
- 50% of people over age 30 years will have CFRD
Cystic fibrosis related diabetes (CFRD) is Common!

![Graph showing prevalence of CFRD](image)

Age (years)

Prevalence (%)

- FH: fasting hyperglycemia
- FH+ FN:
- CFRD total
- FH:
- FN:

Moran et al. Diabetes Care 2009

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CF glucose tolerance categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Fasting blood glucose</th>
<th>2 hr post-prandial glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal glucose tolerance</td>
<td>&lt; 110 mg/dL</td>
<td>&lt; 140 mg/dL</td>
</tr>
<tr>
<td>Impaired glucose tolerance</td>
<td>110 - 125 mg/dL</td>
<td>140-199 mg/dL</td>
</tr>
<tr>
<td>CFRD without fasting hyperglycemia</td>
<td>&lt; 126 mg/dL</td>
<td>&gt; 200 mg/dL</td>
</tr>
<tr>
<td>CFRD with fasting hyperglycemia</td>
<td>≥ 126 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

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Etiology of CFRD

- Pancreatic insufficiency
- Insulin deficiency
- Insulin resistance
  - Particularly when ill or with steroids
<table>
<thead>
<tr>
<th></th>
<th>Type 1 diabetes</th>
<th>Type 2 diabetes</th>
<th>CFRD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Acute</td>
<td>Insidious</td>
<td>Insidious</td>
</tr>
<tr>
<td>Peak age of onset</td>
<td>Children &amp; adolescents</td>
<td>Adults</td>
<td>18-24 years</td>
</tr>
<tr>
<td>Antibody +</td>
<td>Yes</td>
<td>No</td>
<td>Probably No</td>
</tr>
<tr>
<td>Insulin secretion</td>
<td>Eventually absent</td>
<td>Decreased</td>
<td>Severely decreased but not absent</td>
</tr>
<tr>
<td>Insulin sensitivity</td>
<td>Somewhat decreased</td>
<td>Severely decreased</td>
<td>Somewhat decreased</td>
</tr>
<tr>
<td>Treatment</td>
<td>Insulin</td>
<td>Diet, oral medication, insulin</td>
<td>Oral initially and insulin</td>
</tr>
<tr>
<td>Microvascular Complications</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes but less</td>
</tr>
<tr>
<td>Macrovascular Complications</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cause of Death</td>
<td>Cardiovascular disease, Nephropathy</td>
<td>Cardiovascular disease</td>
<td>Pulmonary disease</td>
</tr>
</tbody>
</table>
Question: Why do we care if CF patients have diabetes?

- They already are burdened with complex medical cares
- Some would argue that they may not live long enough to develop diabetes microvascular complications

**WE care because diabetes increases morbidity and mortality!**
Clinical Signs and Symptoms of Diabetes in CF

- Polyuria or polydipsia
- Failure to gain or maintain weight despite nutritional intervention
- Chronic decline in pulmonary function
- Failure to grow
- Delayed progression of puberty

CFF 2010 Consensus Statement: CFRD Screening in Outpatients

- Annual screening with an oral glucose tolerance test (OGTT) in the well-state starting by age 10y
  - Repeat if consistent with CFRD
- Home glucose monitoring
  - If sick: intravenous antibiotics or systemic glucocorticoids
  - During overnight enteral feeds (monthly, 2-hours into feed and 1 hour after feed).

CFF 2010 Consensus Statement

Other measures not recommended for routine screening

- HbA1c > 6.5 is consistent with CFRD, but HbA1c < 6.5 does not exclude
  - HbA1c can be used to follow CFRD control
  - Fasting glucose
    - Fasting glucose above 126 is a late finding in CFRD
Why is it important to treat CFRD?

- Untreated diabetes causes:
  - Muscle wasting
  - Weight loss
  - Reduced ability to fight infection
  - Decreased PFTs
  - Worse survival
  - Greater chance of lung transplant

Why is it important to treat CFRD?

- Insidious decline in pulmonary function and weight (BMI) precedes diagnosis of diabetes by about 6 years
  - Reversible

Management of CFRD
It Takes a Village

Management of CFRD
- BEST accomplished in a Team Setting
  - Patient and Family
  - Pulmonary Team
  - Endocrine Team

Management of CFRD
- Blood glucose monitoring
- Nutrition
- Oral medications
- Insulin
**Blood glucose monitoring:**

- **Glucometer**

  - Goal to keep 2 hour post-prandial blood sugars less than 140 mg/dl
  - Monitoring
    - Fasting blood sugar
    - 2 hour post-prandial after meals
    - Premeal blood sugar if taking insulin
    - In the middle of overnight GT feed

**Nutrition**

- Goal to optimize calorie and fat consumption
- High caloric diet: 120-150% RDA
- High fat
- High sodium: > 4000mg/day
- Replace excessive amounts of sweetened beverages with nutrient-dense calories

**Nutrition**

- Carbohydrates
  - Spread throughout the day
  - Insulin to carbohydrate ratios: matching insulin to carbohydrates consumed
Oral medications

- Improving quality of life!

Oral medications

- Enhance insulin secretion
- Used by 12% of pediatric endocrinologists to treat CFRD
- More commonly prescribed by adult physicians
- Sulfonylureas *not* associated with greater declines in pulmonary function, BG control, or nutritional status when compared to insulin in treatment of CFRD

Oral Medications: Repaglinide (Prandin)

- An oral blood glucose-lowering drug of the meglitinide class
- Similar action to sulfonylureas
- Glucose dependent insulin secretion
- Peak plasma drug levels occur within 1 hour of ingestion
- Can cause hypoglycemia in some females
Repaglinide (Prandin)
- Use when HbA1c less than 8
- Not approved for use in pediatrics
- Can cause hypoglycemia in some females

Insulin
- Initially may only be necessary during pulmonary exacerbation while hospitalized with IV antibiotics and steroids
- May be necessary for hyperglycemia with overnight GT feeds

Insulin
- Short acting (Novolog, Humalog)
  - Onset: 5 minutes
  - Peak: 30 minutes
  - Duration: 2-3 hours
- Intermediate
  - NPH
  - Peak: 4-5 hours
  - Duration: 8-10 hours
Insulin

- Long-Acting (Lantus, Levemir)
  - “basal”
  - Onset: 4-6 hours
  - Duration: 24 hours (for some children only 12-18 hours)
- Premixed:
  - 70 NPH/30 Regular
- Insulin Pump (Novolog/Humalog)
  - Basal and Bolus

Impaired Glucose Tolerance

- 2 hour PP Blood Sugar (140-199)
- Normal HbA1C (less than 6%)
- Plan:
  - Monitor fasting sugars and 2 hr PP
  - F/u CFRD clinic
  - Teaching: glucometer training

CFRD without fasting hyperglycemia

- Fasting blood sugar < 126 mg/dl
- Normal or mildly elevated HbA1c
- Random blood sugar over 200 x 3 especially after meals or tube feedings, OR abnormal OGTT
- No steroids
CFRD without Fasting Hyperglycemia

- Plan:
  - > 10 yo, Prandin 0.5 mg –4mg TID with meals
  - or Humalog/Novolog with meals NPH/Regular
  - or 70/30 for overnight GT feeds
  - < 10yo
  - Humalog/Novolog with meals and large snacks
  - NPH/Regular or 70/30 for overnight GT feeds

CFRD with Fasting Hyperglycemia

- Fasting blood sugar > 126 mg/dl
- Elevated HbA1c (above 8)
- Abnormal OGTT, random blood sugar,
  - or 2 hr PP blood sugar
- No steroids

CFRD with Fasting Hyperglycemia

- Plan:
  - Lantus/Levemir and Humalog/Novolog,
  - NPH and Humalog/Novolog, or 70/30
  - Goal to move towards insulin pump
CFRD with Fasting Hyperglycemia

- Teaching Plan:
  - CFRD teaching packet
  - Home blood glucose monitoring
  - May admit for insulin administration/teaching

The Hospitalized CF Patient

- Extremely insulin resistant!
- Established diabetics require 2-3x usual insulin dose
- New onset child with diabetes: start insulin if FBG > 126 or 2 hour PP > 200 after 2-3 days hospitalization
- Need to back off quickly on insulin as patient recovers

Psychosocial Issues
Psychosocial Issues

- Diabetes worsens overall prognosis
- Families know the statistics for prognosis worsens with diabetes
- Diabetes greatly complicates already complex medical management

Role of APN

- Diabetes Management
  - Goal is to have patients become independent in taking care of CF diabetes
  - Oversee education – 2-3 days intensive days of education when 1st diagnosed
Role of APN

- Insulin dose adjustment and monitoring
  - Phone/email follow-up to review blood sugars and insulin doses
  - Schedule times to check-in

Role of APN

- Case management
  - Glucometer
  - Prescriptions
  - Insulin pumps
  - Fight with insurances, prior authorizations, letters of medical necessity!!

Role of APN

- Care Coordination
  - Between departments (Endocrine, CF, GI, transplant)
  - Pull it all together for the patient (clinic visits, homecare, school)
Case Study # 1

- AB is a 18 yo male with CFRD
- Diagnosed 6 mos earlier at Yale and started on Lantus/Novolog during pulmonary exacerbation
- Currently on Lantus 3 units at bedtime, Novolog prn high sugars
- Flat affect, depressed, had not been to school in 1 month, trouble maintaining weight
- FBS 100-116, 2 hr PP between 180-240, HgbA1c = 6.6

Case Study # 1

- Stopped Lantus, started Prandin 0.5 mg before meals and snacks
- F/u 1 week with BS logs
- 3 months later:
  - Weight improved by 3 kg
  - PFTs remained the same: 98%
  - HgbA1c= 6.4
  - Perfect school attendance for 3 mos, starting college in fall, interactive and making eye contact

Case Study #2
Case Study # 2

- RS is a 15 yo male with CFRD
- Dx with CFRD during hospitalization for pulmonary exacerbation, currently on steroids
- FBS = 150-160's, 2 hr PP BS= > 200,
  HgbA1c= 10.8
- PFTs= 88 %, weight loss of 5 kg

Case Study #2

- Started on 70/30 insulin BID
- 2-3 days intensive education/training in hospital
- Steroids were stopped and sugars still remained high
- Transitioned to Lantus/Novolog 4 weeks later for flexibility

Case Study #2

- 5 months later:
  - Started insulin pump
  - HgbA1c = 6 %
  - PFTs= 104%
  - Weight increased: 7kg
  - Happy!
Case Study #3

JM is a 14 yo female with CFRD who gets 8 hour overnight GT feed.
- Required insulin while on oral prednisone while hospitalized.
- Blood glucose improved/normalized with discontinuation of Prednisone and no additional insulin needed.

Case Study #3

- In clinic: Hgba1c= 5.4, weight = 42.6 kg
- 2 hour pp = 100-120 during the day but above 200 during overnight feed
- PFTs= 41%
- Began 70/30 before overnight feed
- Mother concerned about polyuria/polydipsia
- during the day—ipro CGMS to evaluate
Case Study #3

- 5 day ipro CGMS revealed:
  - Overall Hyperglycemia = 10%,
  - within range = 90%, Hypoglycemia = <1%
  - Increased 70/30 with overnight GT feed
  - No insulin at this time during day
  - 1 month later: Hgba1c=5.3, weight= 44 kg

Many Questions Remain.....

- Role of treatment of impaired glucose tolerance in children with CF and poor growth or nutritional status
- Female sex and CFRD