

**Stanford CF Center  
Cystic Fibrosis Related Diabetes  
(CFRD)**



**AN UPDATE ON CFRD AND  
OUR CENTER'S PROTOCOL:  
KEEPING IT SHORT AND SWEET!**

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# Cystic Fibrosis Related Diabetes:



**Type 1:  
lack of  
insulin  
secretion**

**Type 2:  
insulin  
resistance/  
decreased  
insulin  
secretion**

# CFRD Is a Distinct Form of Diabetes:



**Type 1**

**Type 2**

**CFRD**

Most common age of onset	<b>&lt;20</b>	<b>&gt;40</b>	<b>22-24</b>
Usual body habitus	<b>Normal</b>	<b>Obese</b>	<b>Normal</b>
Insulin Secretion	<b>↓</b>	<b>↓</b>	<b>↓</b>
Insulin Sensitivity	<b>Absent</b>	<b>↓↓↓</b>	<b>↓</b>
Autoimmune etiology	<b>↓</b>	<b>No</b>	<b>↓</b>
Ketoacidosis	<b>Yes</b>	<b>Rare</b>	<b>No</b>
Microvascular complications	<b>Yes</b>	<b>Yes</b>	<b>Rare</b>
Macrovascular complications	<b>Yes</b>	<b>Yes</b>	<b>Yes</b>
	<b>Yes</b>		<b>No</b>

# Microvascular Complications in Individuals with Diabetes > 10 Years Duration:

<b>Complication</b>	<b>CFRD</b>	<b>T1D/T2D</b>
Retinopathy	15%	60%
Nephropathy	16%	20-30%
Neuropathy	50%	50%
Gastropathy	50%	50%
Macrovascular	0%	~60%

# Clinical Signs and Symptoms of CFRD:

- Excessive thirst or excessive urination
- Failure to gain or maintain weight despite nutritional intervention
- Failure to grow
- Delayed progression of puberty
- Chronic decline in pulmonary function

# Outcomes:

- **Reduced survival**

- In a study of 448 people with CF, less than 25% with diabetes survived to age 30, whereas nearly 60% of people without diabetes reached this age

Finkelstein et al *J Pediatr* 1988

- **Decreased pulmonary function**

- Cross sectional analysis of 7,566 people enrolled in the European Epidemiologic Registry of CF found lower FEV<sub>1</sub> in those with DM vs those without DM at all ages (72% vs 52%)

Koch et al *Pediatr Pulmonol* 2001

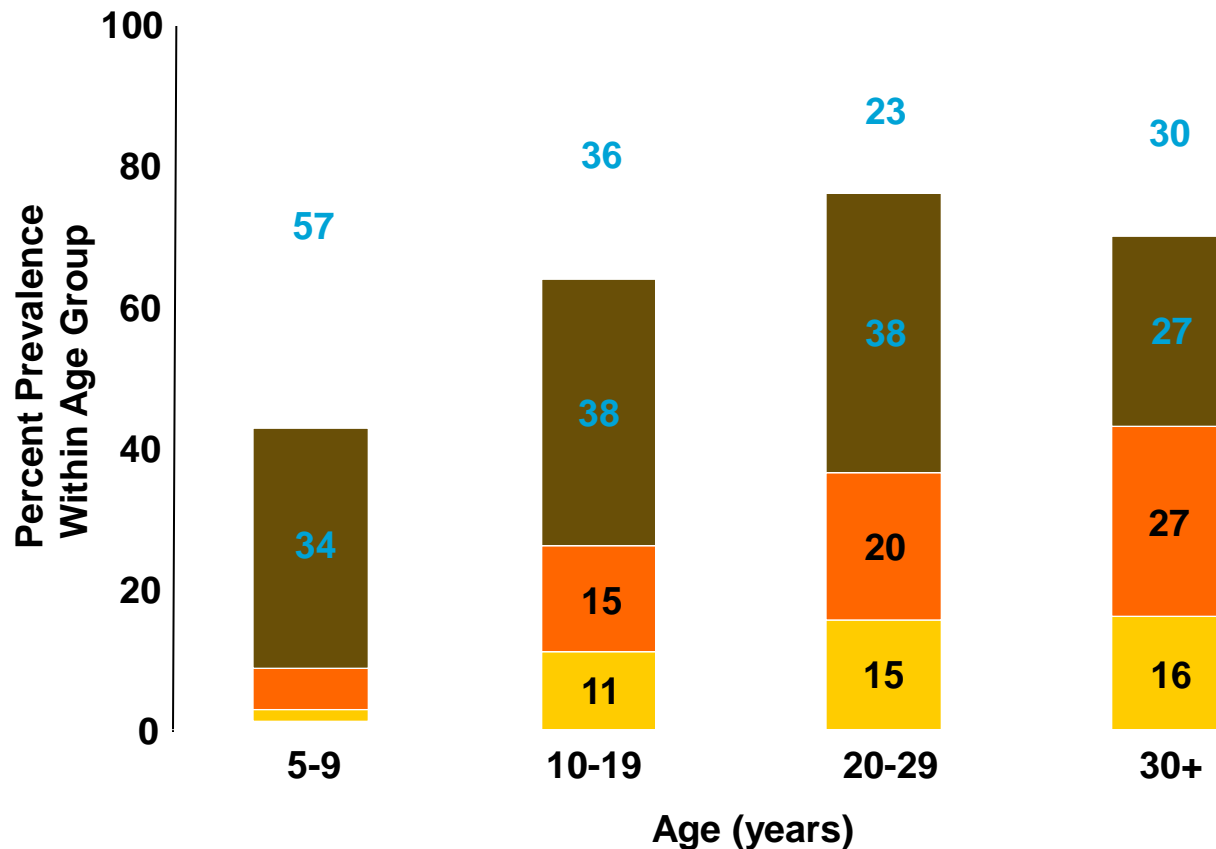
# Oral Glucose Tolerance Test (OGTT)

- **Fasting, 30 minute, 1 hour, 2 hour blood draws after glucose beverage**
- **Most sensitive way to detect CFRD without fasting hyperglycemia**
- **Early Identification is KEY!**
  - High risk for progression to fasting hyperglycemia
  - High risk for excessive decline in pulmonary function

Moran A, et al. *Diabetes Res Clin Pract.* 1999.

Milla CE, et al. *Am J Respir Crit Care Med.* 2000.

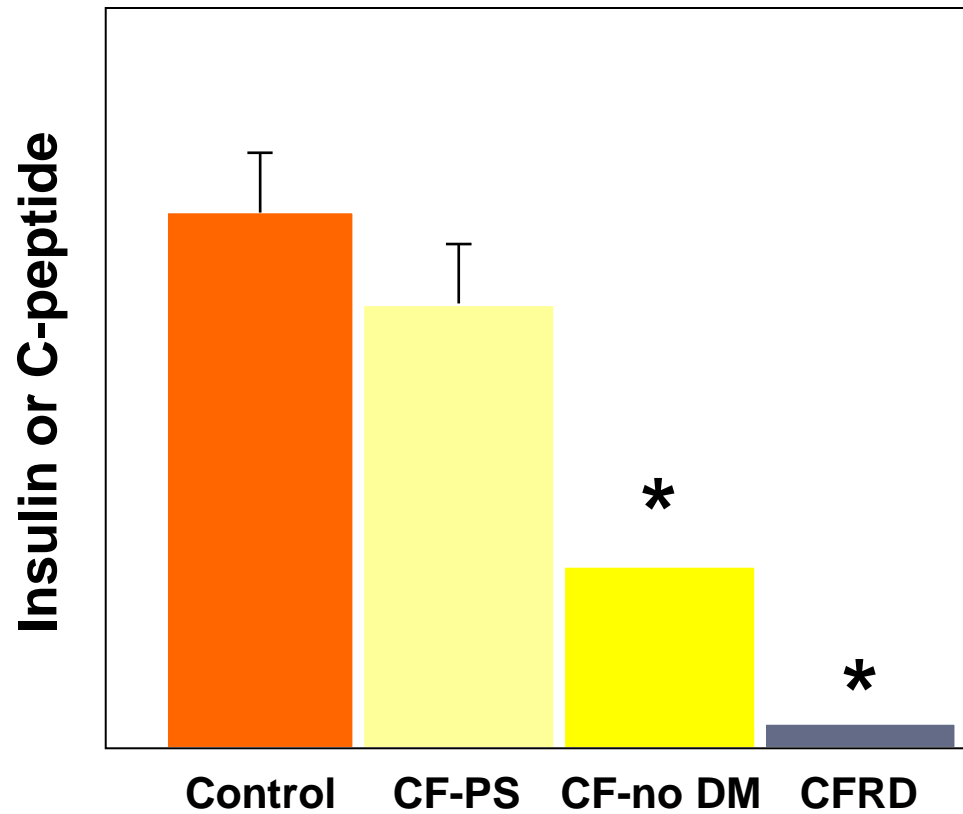
# Glucose Tolerance Prevalence in Individuals with CF



- Normal glucose tolerance
- Impaired glucose tolerance
- CFRD without fasting hyperglycemia
- CFRD with fasting hyperglycemia



# Insulin Secretion:



PS=pancreatic sufficient  
DM=diabetes mellitus

Moran A, et al. *J Pediatr.* 1991

\*  $P < 0.001$  vs control

# Insulin Therapy Improves BMI in CFRD Without Fasting Hyperglycemia:

- N= 81
- Individuals with CFRD without fasting hyperglycemia were treated with insulin vs. Repaglinide or placebo
- Insulin group showed improved BMI after one year of therapy whereas the group treated with Repaglinide did not

Moran A. et al. *Diabetes Care*. 2009.



## Position Statement

Published in *Diabetes Care*, December 2010

Joint effort from the American Diabetes Association, CF Foundation, and endorsed by the Pediatric Endocrine Society

## Screening Recommendations

- Use of A1C not recommended
- Screening: 2 hour OGTT
- Begin annual screening at age 10
- In-patient screening: Fasting, 2 hour post-prandial BS x 48 hours
- Screening for patients on continuous enteral feeds at time of gastrostomy feeding initiation, then monthly using SMBG



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## Diagnosis Recommendations

- 2 hour OGTT plasma glucose  $\geq$  200 mg/dl
- Fasting plasma glucose  $\geq$  126 mg/dl
- A1C  $\geq$  6.5%
- Test on 2 separate days to rule out laboratory error
- Diagnosis can be made during acute illness, when abnormal fasting plasma glucose or 2 hour post prandial levels persist for greater than 48 hours



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## Management Recommendations

- Refer to Endocrine (initially should be seen quarterly)
- Treatment with insulin
- Blood sugar monitoring minimum of three times daily
- Follow A1C quarterly (goal <7%)
- Nutrition management with carbohydrate counting (no calorie restriction)



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## Diabetes Complications

- Education regarding symptoms, prevention and treatment of hypoglycemia
- Measure blood pressure at every diabetes visit
- Annual monitoring for microvascular complications ( $\geq 5$  years )
- Annual lipid profile (Pancreatic sufficient patients or if risk factors present)

# LPCH CF Center Protocol



- **Annual screening:** 6 years and older with concurrent insulin levels
- **Home BG monitoring:** Individuals with impaired glucose tolerance
- **Referral to Endocrine:** Individuals with CFRD with and without fasting hyperglycemia
- **In-patient monitoring:**
  - Fasting, 2 hour post-prandial BG x 48 hours
  - 2 am, immediately post overnight GT feeds for individuals with newly placed gastrostomy tube feedings

# What does more aggressive management mean?



- Routine screening with annual OGTT for patients aged  $\geq 6$  years
- Careful inpatient glucose monitoring and use of insulin as needed
- Early institution of intensive insulin therapy has become more routine in the last 5 years
- Pre-meal insulin is prescribed for those with CFRD without fasting hyperglycemia



# Summary:



- CFRD is a challenging disease to diagnose and treat
- Earlier screening
- Improve the health and well being of our patients and families

# Questions?



Thank you!

