Pancreatic Diabetes: Diagnosis and Management

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Disclosures

- Consulting/advising: Bayer, Boehringer Ingelheim, Jaeb Center, Mannkind, NIH, Novo Nordisk, Provention Bio
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Learning Objectives

- Recognize the epidemiology, including regional variability, in the prevalence of Type 3c diabetes.
- Identify the pancreatic disorders that cause Type 3c diabetes.
- Learn the diagnostic criteria for pancreatic exocrine insufficiency, and for Type 3c diabetes.
- Implement nutritional and medication management for optimal results in Type 3c diabetes.

Where did Type 3c Diabetes (AKA Pancreatic Diabetes) get its name?

Table 1—*Etiologic classification of diabetes mellitus*

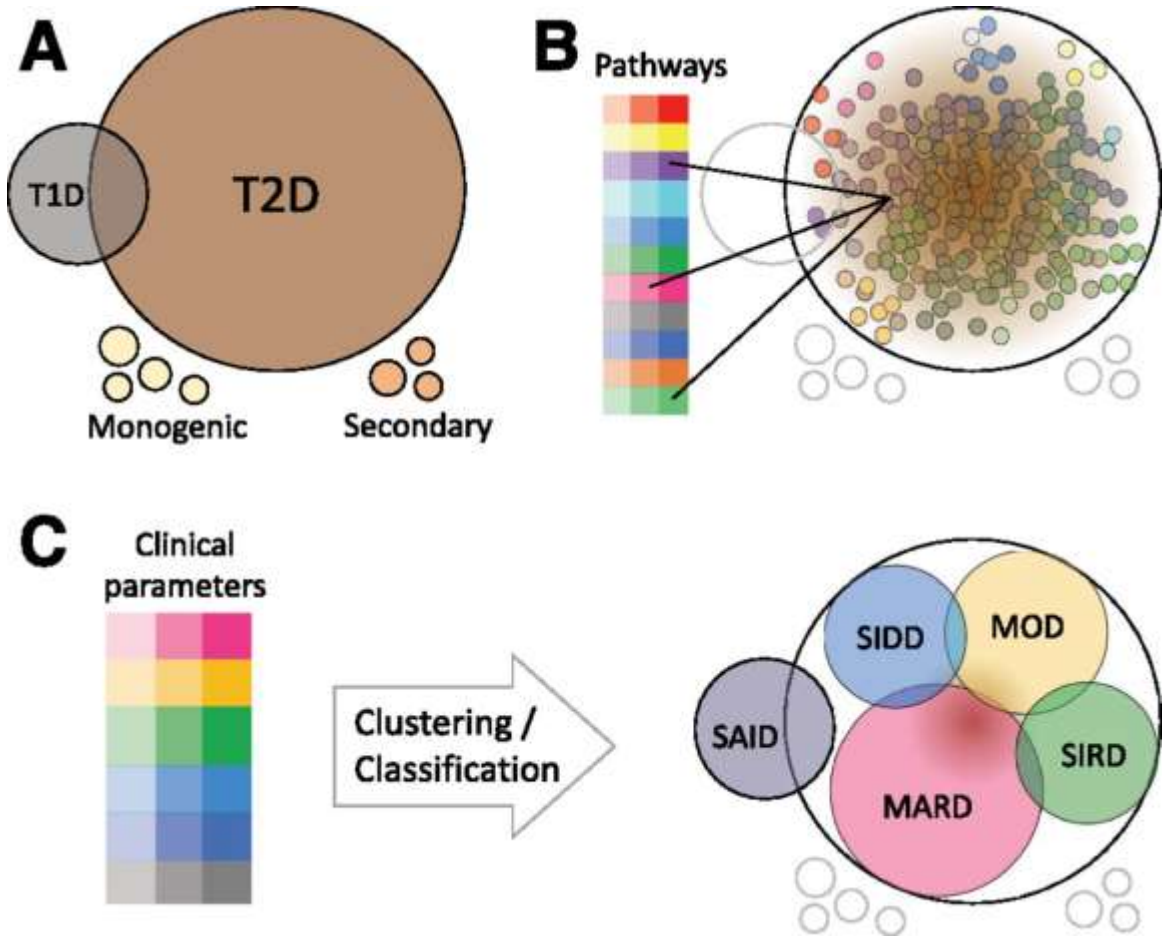
I. Type 1 diabetes* (β-cell destruction, usually leading to absolute insulin deficiency)
  A. Immune mediated
  B. Idiopathic
II. Type 2 diabetes* (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III. Other specific types
  A. Genetic defects of β-cell function
    1. Chromosome 12, HNF-1α (MODY3)
    2. Chromosome 7, glucokinase (MODY2)
    3. Chromosome 20, HNF-4α (MODY1)
    4. Mitochondrial DNA
    5. Others
  B. Genetic defects in insulin action
    1. Type A insulin resistance
    2. Leprechaunism
    3. Rabson-Mendenhall syndrome
    4. Lipoatrophic diabetes
    5. Others
  C. Diseases of the exocrine pancreas
    1. Pancreatitis
    2. Trauma/pancreatectomy
    3. Neoplasia
    4. Cystic fibrosis
    5. Hemochromatosis
    6. Fibrocalculous pancreatopathy
    7. Others

Table 1 in the ADA Guidelines 2003

Subtypes of Type 2 Diabetes: Can Clusters be Identified?

ANDIS: All New Diabetics in Scania.

- Diabetes cohort started in 2008, purpose of studying diabetes heterogeneity
- >20,000 individuals, >90% of newly diagnosed patients
- Measure GADA and C-peptide, in addition to
- Age of onset, BMI, A1c,
- HOMA2-B and HOMA2-IR



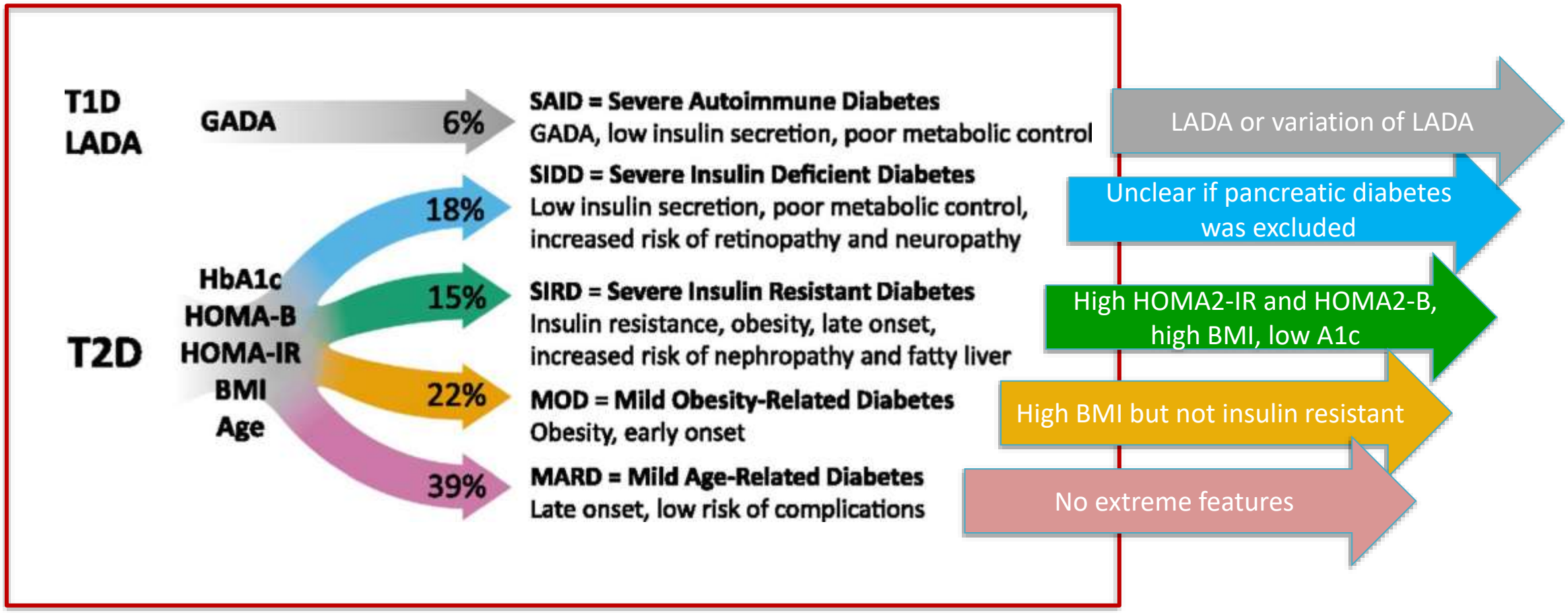
2000 Diabetes Volume 69, October 2020

Subtypes of Type 2 Diabetes Determined From Clinical Parameters

Emma Ahlqvist,[1] Rashmi B. Prasad,[1] and Leif Groop[1,2]

Diabetes 2020;69:2086–2093 | https://doi.org/10.2337/db20-0001

Subtypes of Type 2 Diabetes



Cohorts were followed for complications

Alqvist E, *Diabetes*, 2020

Case 1: Patient on the IP Diabetes Service

CC:	33 y/o female with abdominal pain, nausea/vomiting
PMH:	Hereditary pancreatitis, chronic abdominal pain
PSxH:	Partial pancreatectomy (1/3 distal) and jejunostomy, splenectomy, cholecystectomy, c-section (partial sacral agenesis of fetus)
Meds:	Levemir 10U daily, Novolog 4U TIDAC, PO Dilaudid, pregabalin, omeprazole, sertraline
SH:	No tobacco/alcohol/recreational drug use; married, 2 kids (2, 6)
FH:	Father – pancreatitis; Grandfather – T1DM
ROS:	+diarrhea/steatorrhea
PE:	T 36.9, P 74, BP 107/75, 59.1 kg (BMI 21.70)
	+abdominal tenderness

Case 1: Patient on the IP Diabetes Service

- Labs - Hgb A1C: 15.1%
  Lipase: <3 Units/L (10-99)
  Vitamin A: 17.1 mcg/dL (32.5 – 78.0)
  Vitamin D, 25-OH: 14 ng/mL (30 – 80)
  Vitamin E: 1.9 mg/L (5.5 – 17.0)
  Vitamin K: <0.03 ng/mL (0.10 – 2.20)
- Imaging - CT abd/pelvis: atrophic remnant pancreas with calcifications
- <u>Pancreatitis History:</u>
  - First episode at age 5
  - Genetic Testing: R122H PRSS1 variant (AD)
  - Abdominal pain impeded follow-up and medication compliance

Pancreatic Diabetes Mellitus Definition: Diabetes associated with Pancreatic Exocrine Insufficiency (PEI)

Major criteria

- Hyperglycemia
- Presence of exocrine pancreatic insufficiency by fecal elastase-1 or stool fat
- Imaging evidence of pancreatic pathology
- Abse

Minor criteria

- Impaired β-cell function (measured by C-peptide/glucose or HOMA-β)
- No excessive insulin resistance (measured by HOMA-IR)
- Impaired incretin (GIP) or pancreatic polypeptide (PP) secretion
- Low levels of fat soluble vitamins (A, D, E, K)

Hart PA et al. *Lancet Gastroenterol Hepatol,* 2016; Ewald N, Bretzel RG. *Eur J Intern Med,* 2013

EPIDEMIOLOGY

Etiology of diabetes and prevalence of T3cDM varies regionally. Prevalence data are estimates.

- North America, 1 - 5% of all cases of diabetes
- South America, unknown, suspected >10%
- Europe, 4 – 9%
- Southeast Asia, up to 30%
- East Asia, unknown

Chronic pancreatitis occurs in up to 50/100,000 persons in the west, with significant regional variability (high in Russia and Japan due to alcohol), up to 125/100,000 in SE Asia due to fibrocalcific disease

Hart PA, *JOP*, 2008; Ewald N, *Diab Res Clin Prac*, 2013

Misclassification Occurred in 49% of T3cDM Cases

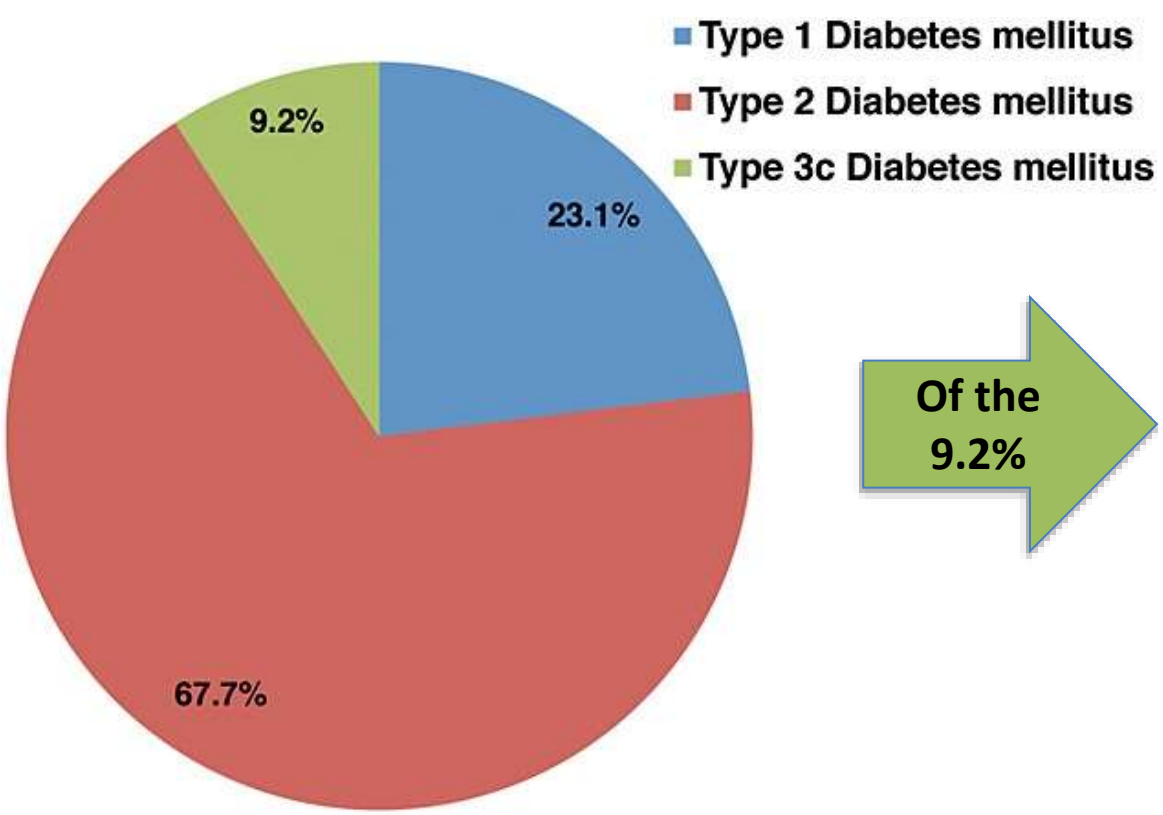
Table 1. Preclassification and reclassification of the different diabetes types

	Reclassified as			
	Type 1	Type 2	Type 3c	Total
Previously classified as				
Type 1	412	13	11	436
Type 2	12	1217	69	1298
Type 3c	4	25	88	117
Not classified	3	10	4	17
Total	431	1265	172	1868

Ewald N, *Diab Res Clin Prac*, 2013

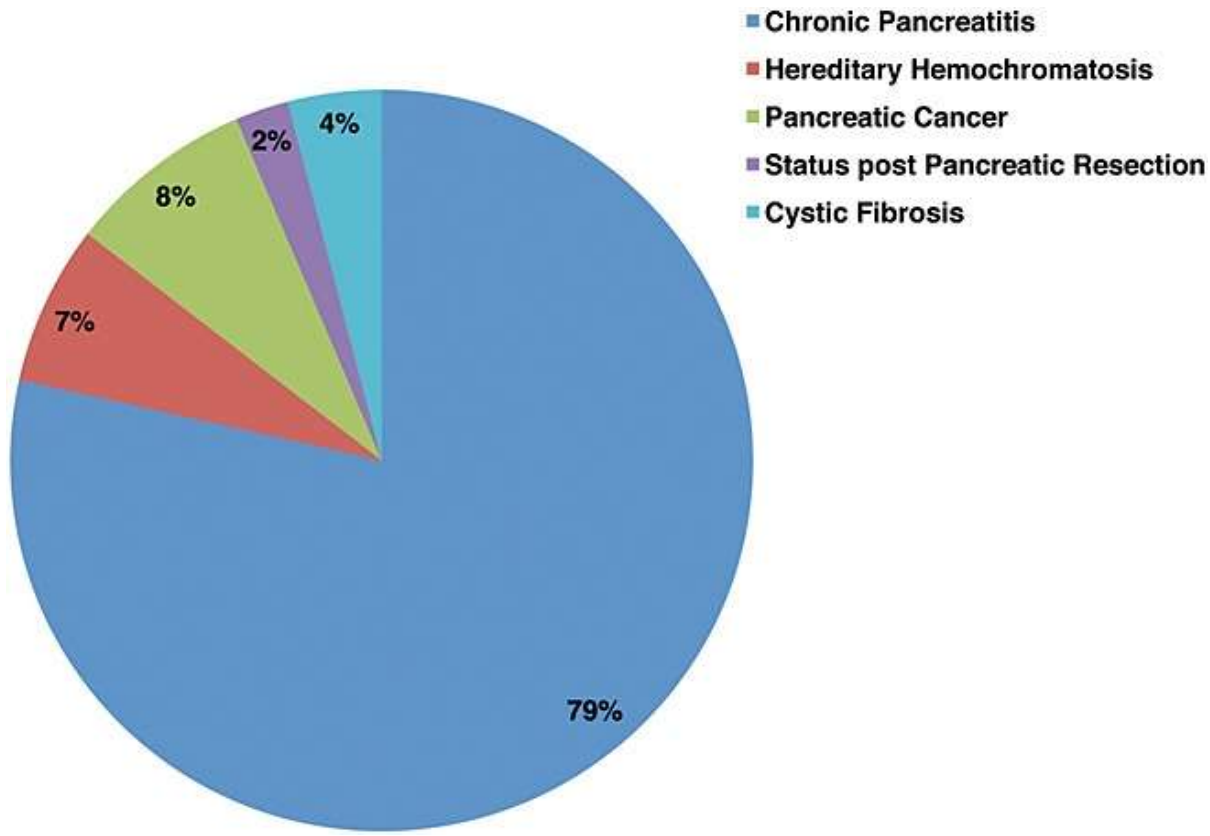
Analysis of 1868 Patients with Diabetes, Germany

After reclassification



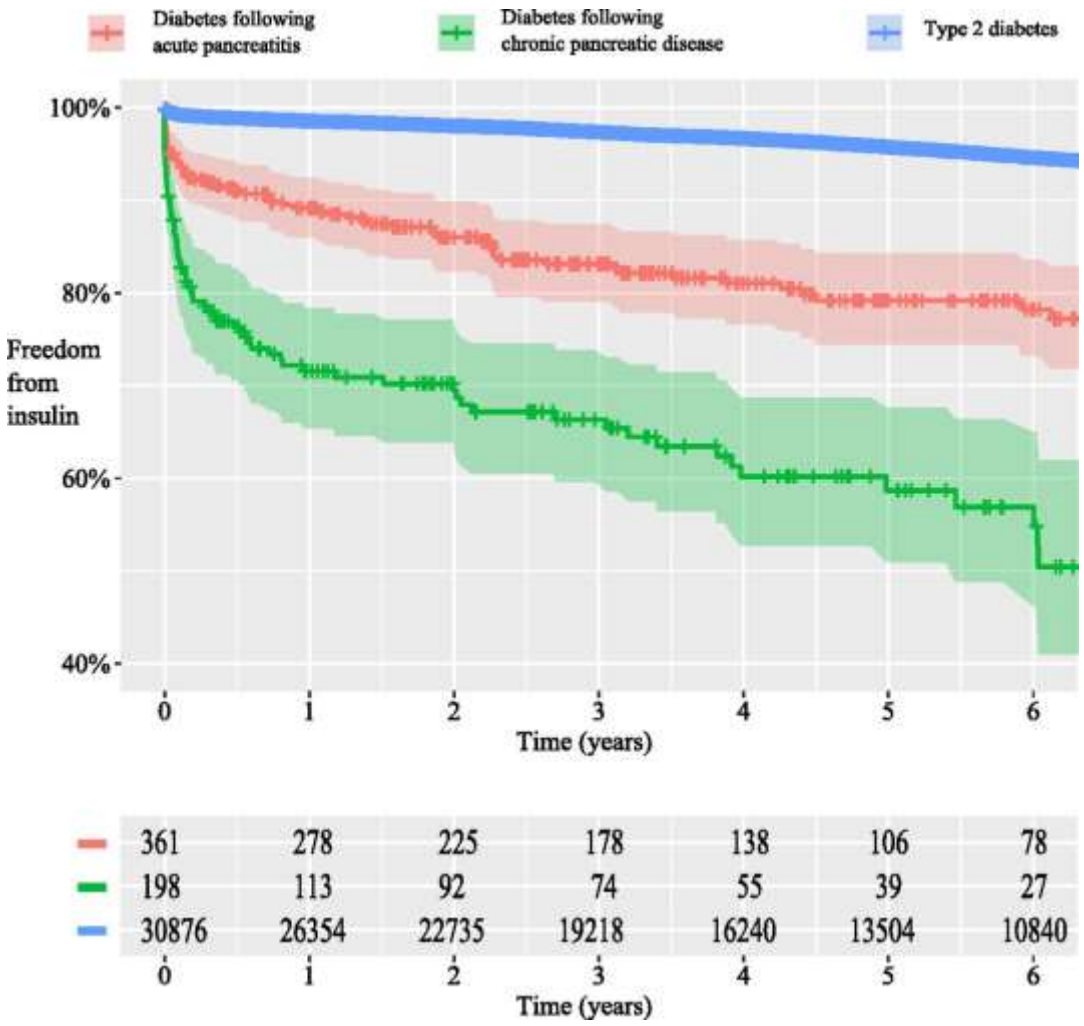
Of the 9.2%

Etiology of Type 3c Diabetes, n=172



Ewald N, *Diab Res Clin Prac*, 2013

Diabetes Diagnosis following Pancreatic Disease



- New diabetes following pancreatic disease diagnosis in UK: 1.8% of all cases of incident diabetes (new T1DM, 1.1%)
- Diabetes following pancreatic disease patients had worse glucose control and progressed to insulin much faster than T2DM

Woodmansey C, *Diabetes Care, 2017*

Pathogenesis of Type 3c Diabetes Mellitus

Infancy

- Pancreatic agenesis

Childhood

- Pancreas divisum
- Genetic pancreatitis
  - PRSS1,2 mutations
  - SPINK1 mutation

Young Adults

- Cystic fibrosis related diabetes
- Carboxyl-ester lipase (CEL) mutation

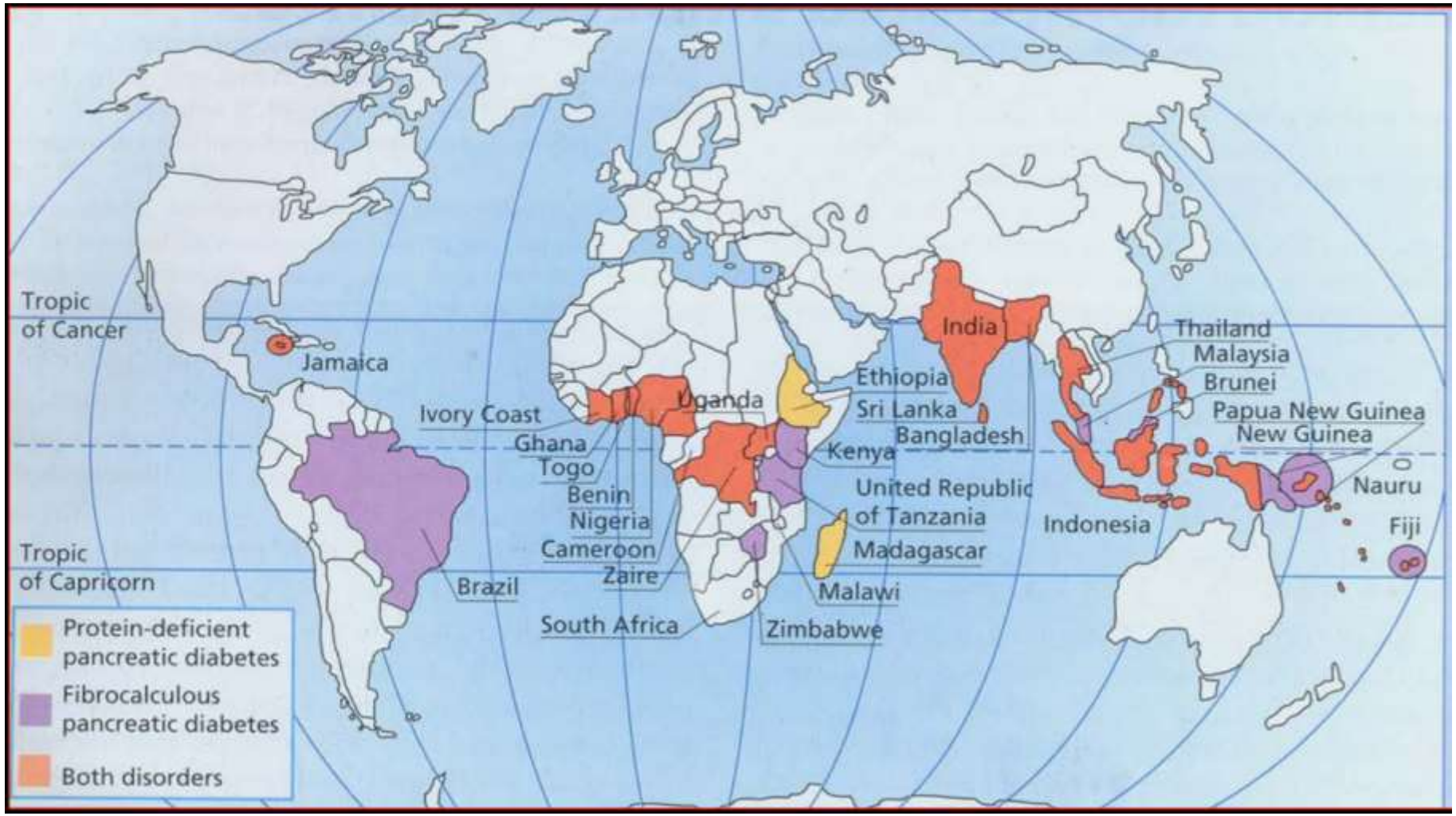
Adulthood

- Acute/Chronic pancreatitis*
  - Alcohol, other toxins
  - Autoimmune (IgG4, idiopathic)
  - Metabolic (high triglycerides)
  - Hemochromatosis
  - Obstructive (gallstone, duct obstruction)
  - Tropical fibrocalcific pancreatitis
- Pancreatic surgery
  - Partial or total pancreatectomy

* Most common

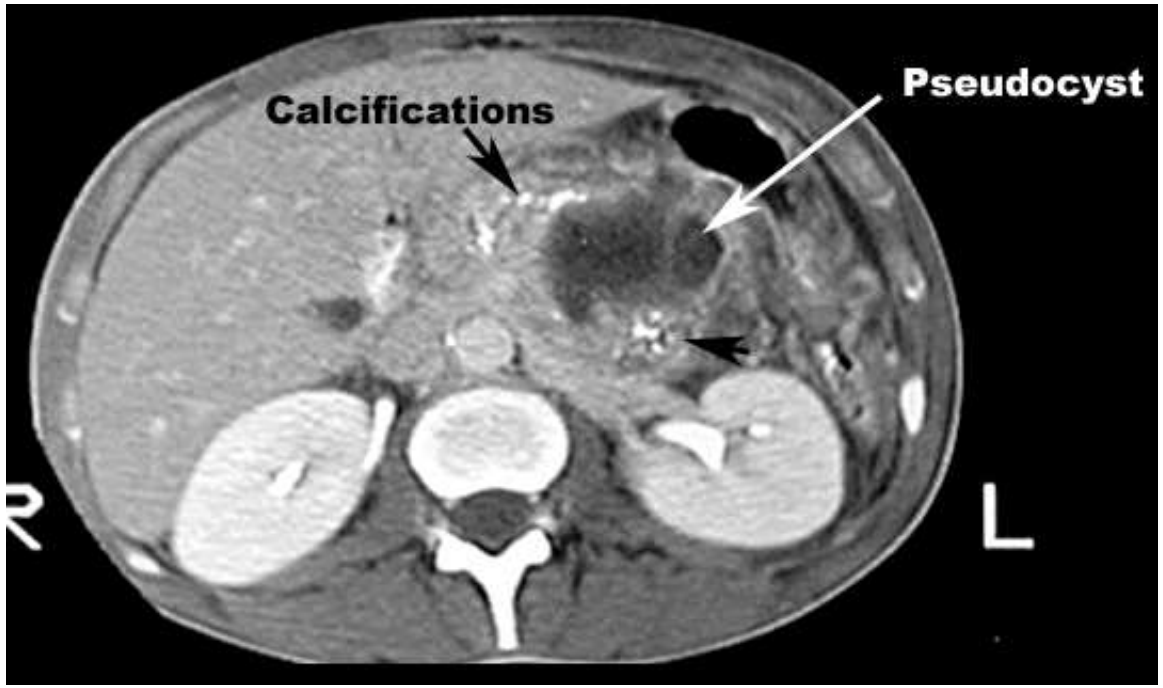
Zhu X, *Pancreas, 2019;* Sholten L, *Surgery,2018*

Protein-deficient and Fibrocalculous Diabetes

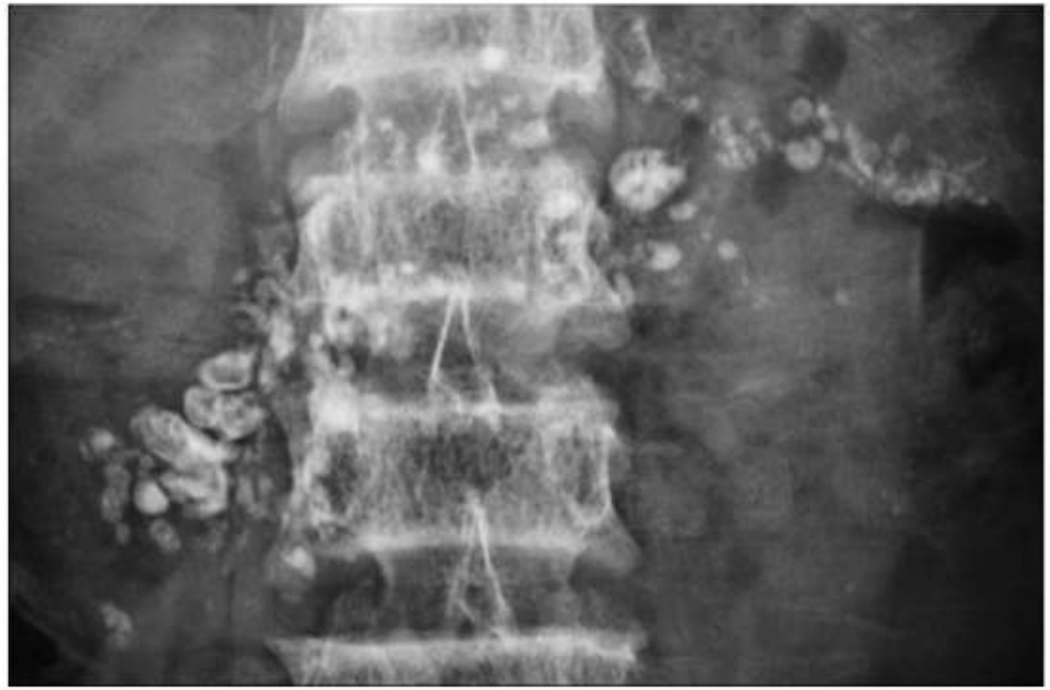


World-wide prevalence, WHO; source: Google Images

Pancreatic Calcification: Mild in chronic pancreatitis, severe in Fibrocalcific Pancreatitis



Chronic Pancreatitis with Pseudocyst



Pancreatic Calcification

- www.stritch.luc.edu; Khuroo M, *JOP*, 2010

Genetic Contributors to Chronic Pancreatitis, Fibrocalcific Pancreatic Disease (FCPD) and PEI

- Genetic alterations in trypsinogen pathway, associated with FCPD
  - Serum protease inhibitor Kazal type 1 (SPINK1)
  - Cationic trypsinogen (PRSS1), activating mutation in trypsinogen gene, autosomal dominant; Anionic trypsinogen (PRSS2)
  - Chymotrypsinogen C (CTRC)
- Other genes associated with PEI
  - Cystic fibrosis transmembrane conductance regulator (CFTR)
  - Regenerating islet-derived genes 1α (REG1A, REG1B)
  - Cathepsin B (CTSB)
  - Calcium sensing receptor (CASR)
  - Carboxyl-ester lipase (CEL)

Pancreatic Exocrine/Endocrine Dysfunction

- 2 extended Norwegian families with exocrine pancreatic insufficiency and diabetes; also mild intermittent abdominal pain but no definitive episodic pancreatitis; neuropathy
- Mutation in the Carboxyl-Ester Lipase (CEL) gene
- Autosomal dominant inheritance, diabetes before age 40.
- The mutation was a single base deletion in the variable number of tandem repeats containing exon 11 of the Carboxyl-Ester Lipase gene.

Raeder. *Nature Genetics* 2006 38(1) 54-62

Pancreatic Exocrine +/- Endocrine Dysfunction

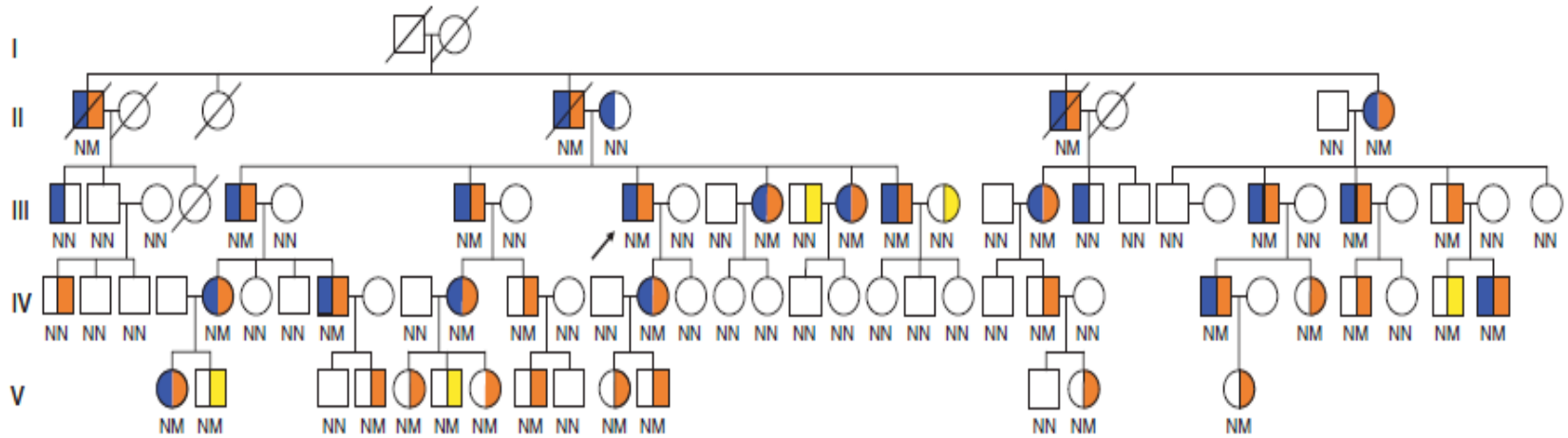


Figure 1 Pedigree of studied branches of Family 1. Severe (red) and moderate (yellow) exocrine pancreatic dysfunction, diabetes or impaired glucose tolerance (blue) are defined in Methods. The proband is indicated by an arrow. NN, no mutation; NM, mutation.

- The incidence of diabetes is < than PEI and appears later in life, however the fatty pancreas replacement is seen early.

PANCREAS EXOCRINE SEVERE

PANCREAS EXOCRINE MODERATE

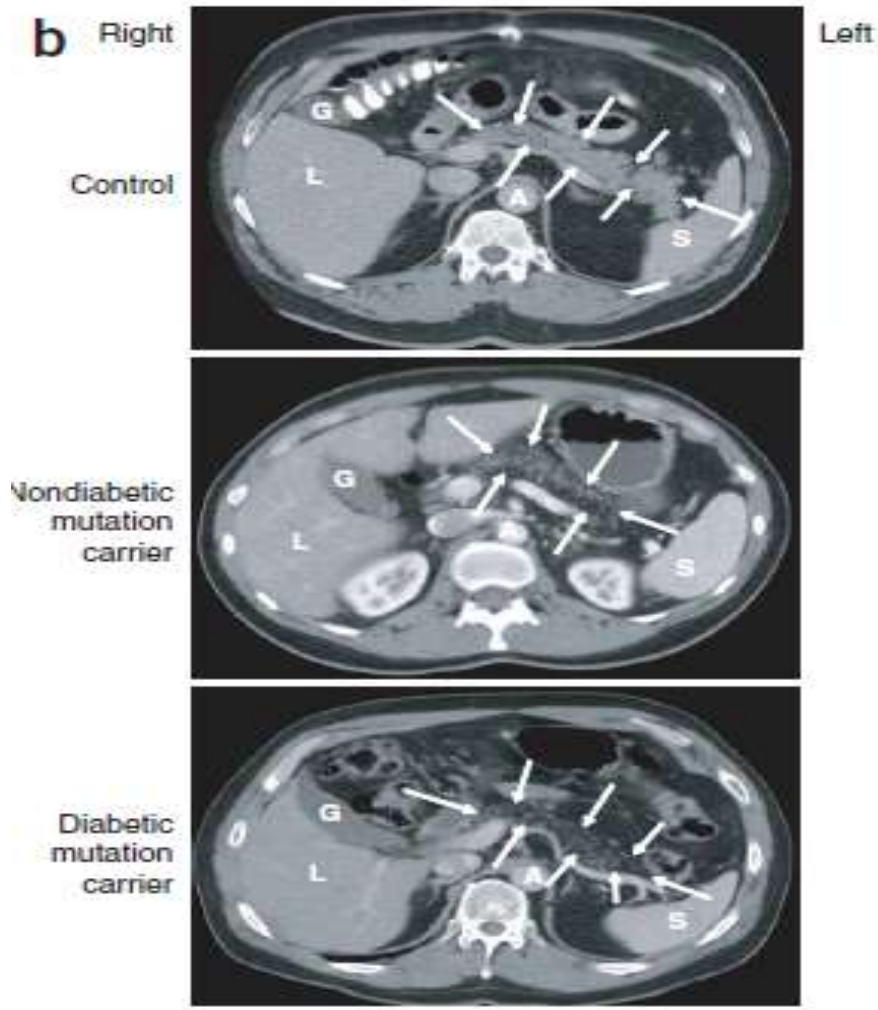
DIABETES/ IGT BLUE

Raeder. *Nature Genetics* 2006 38(1) 54-62

Pancreas Images: Genetic Mutation and T2DM

- Pancreas is smaller in CEL mutation carriers than non-carriers
- Replacement of pancreatic parenchyma with fat is a consistent finding
- Pancreatic lipomatosis can be found in T2DM, Cushings, chronic pancreatitis; Shwachman-Diamond, alcoholic hepatitis

In a large series of Chinese patients (4419) with T2DM, 11% were found to have pancreatic lipomatosis/steatosis and/or pancreatic atrophy



Raeder. *Nature Genetics* 2006 38(1) 54-62; Weng S, *Medicine*, 2018

Autoimmune Causes of Chronic Pancreatitis

- Type 1, IgG4: dense infiltration of plasma cells and sclerosis, can appear as a mass. This condition affects other organs as well and is generally steroid responsive

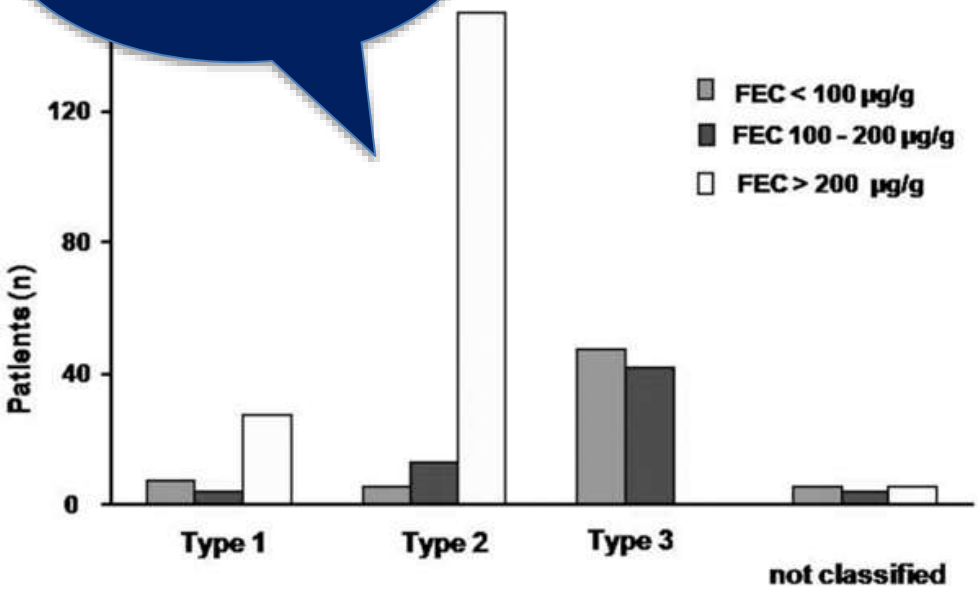
- Type 2, autoimmune pancreatitis: no obstruction or toxins; associated with inflammatory bowel disease or other autoimmune conditions; may not be responsive to steroids

Pancreatic Exocrine Insufficiency (PEI)

- Exocrine pancreatic insufficiency is defined by a deficiency of exocrine pancreatic enzymes resulting in an inability to maintain normal digestion.
- PEI is diagnosed by testing exocrine pancreatic function.
- PEI is typically not clinically significant until the intra-duodenal lipase levels fall below 5-10% of the normal enzyme output.
- Classic presentation: steatorrhea (floating stools, stools sticking to sides of the toilet), weight loss, pain. Patients may present with bone pain from osteomalacia or severe neuropathy. Mild or partial cases may not be symptomatic.
- Many patients are relatively tolerant of PEI and may or may not take pancreatic enzymes. Cost of enzyme replacement can be limiting.

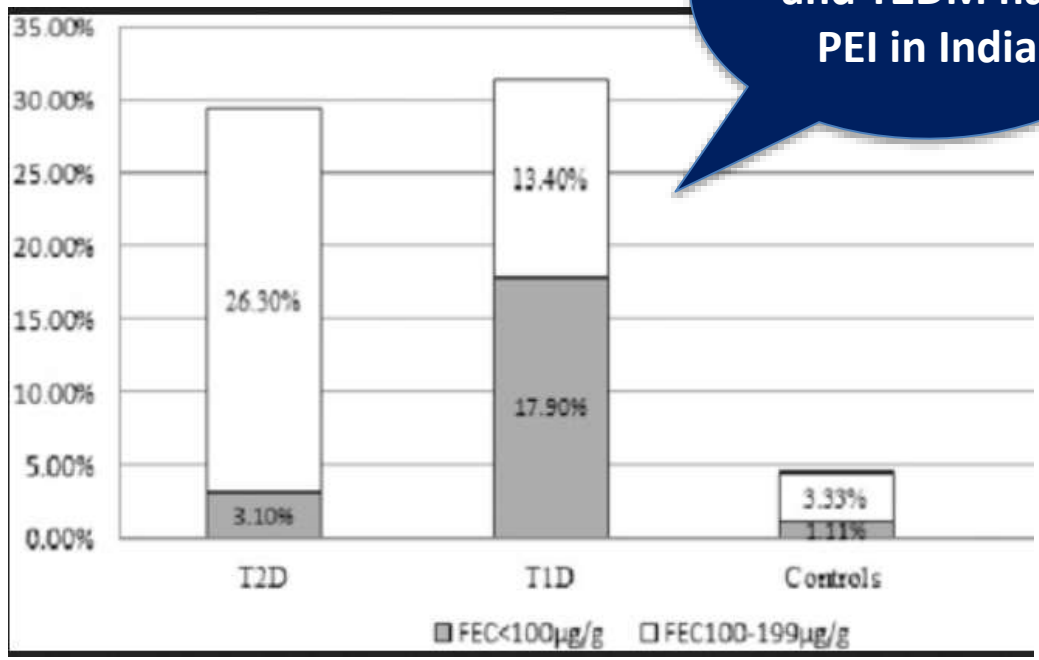
Pancreatic Exocrine Insufficiency (PEI) by Fecal Elastase-1 in Patients with Type 1, Type 2 and T3c Diabetes

5-10% of T1DM and T2DM had PEI in Germany



Germany

30% of T1DM and T2DM had PEI in India



India

Ewald N, *Eur J Med Res,* 2009*;* Shivaprasad C, *Pancreatology,* 2009

Making the Diagnosis of T3cDM

Start with the history: episodes of pancreatitis, pancreatic surgery, known pancreatic disease; timeline for other problems, signs and symptoms of malabsorption

Endocrine Insufficiency

- Fasting glucose/insulin/C-peptide
- OGTT (most sensitive)
- Islet auto-antibodies (absence)
- Mixed-meal stimulated **pancreatic polypeptide**
  - Normal, increases 6 – 8X
  - T1DM, early disease, may increase
  - T2DM, increased basal, stimulated 6-8X
  - T3cDM, low basal, stimulated increase <2X

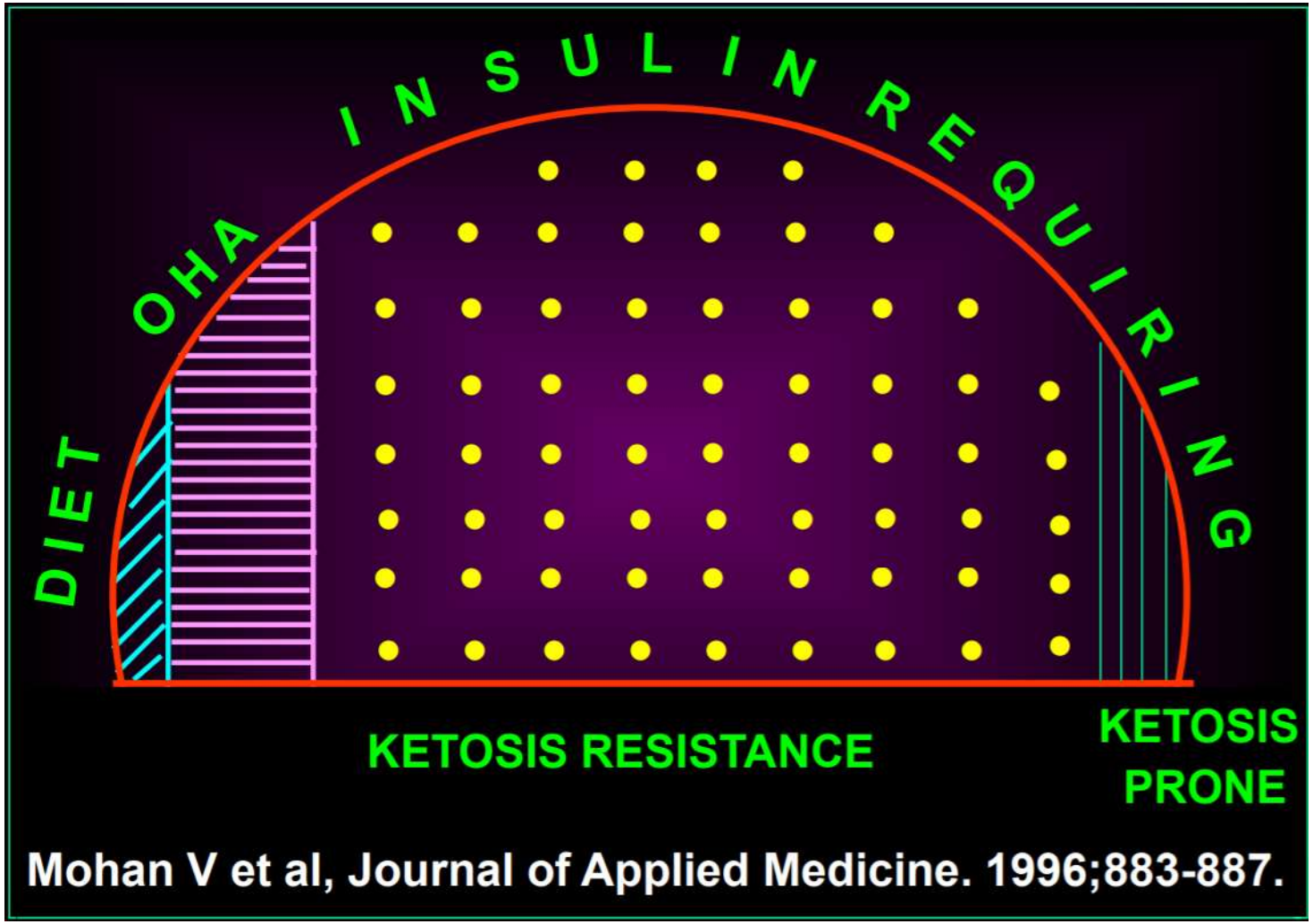
Exocrine Insufficiency

- Stool elastase-1 (mild, <200 mcg/g; severe, <100 mcg/g)
- 3-day fecal fat (>7 grams/100 g stool while on a high fat diet)
- Fat soluble vitamins (low)
  - A, D, E, K
- Imaging of the pancreas
  - Calcification, lipomatosis, atrophy

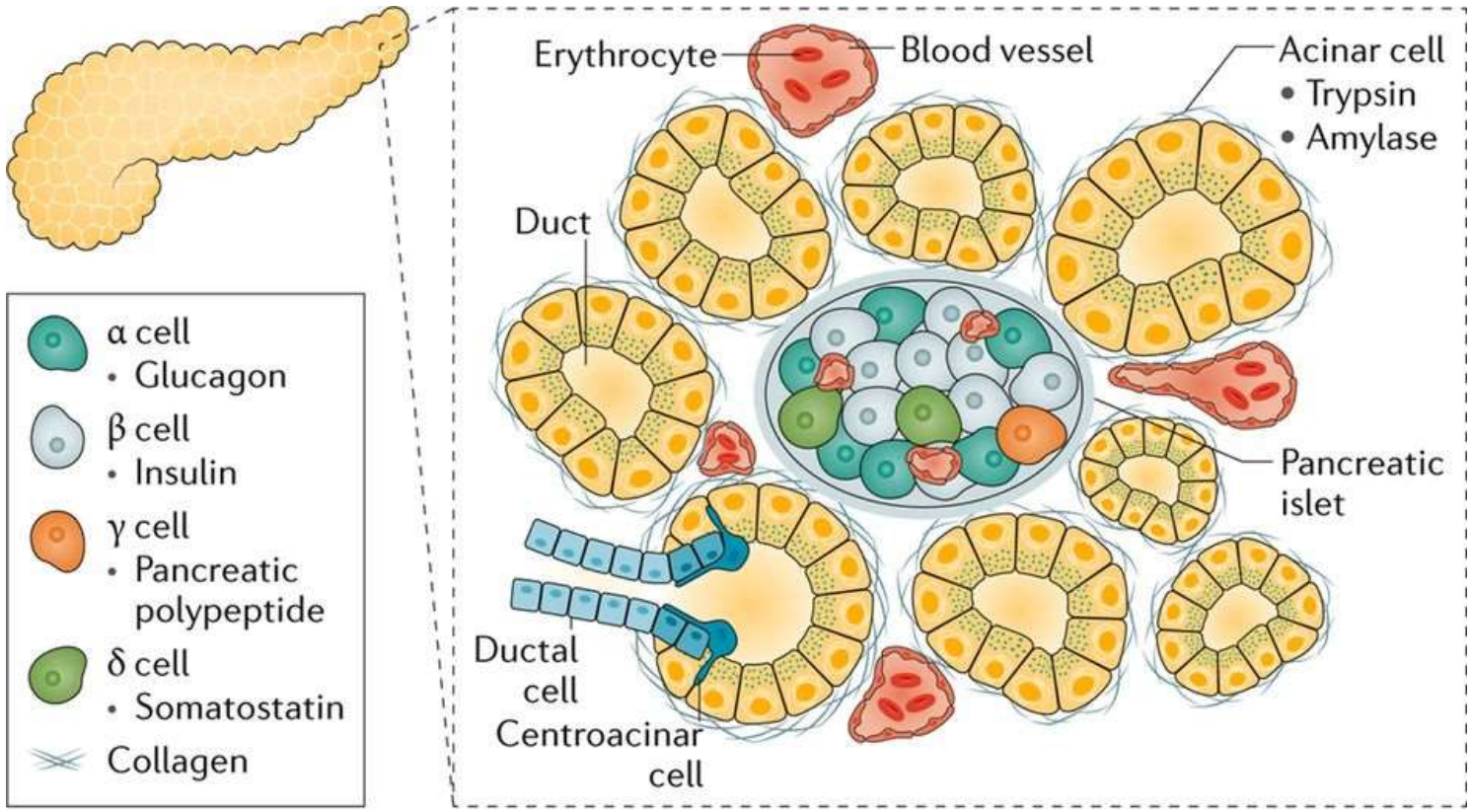
Additional Findings

- Low amylase/lipase

Spectrum of Diabetes in Chronic Pancreatitis

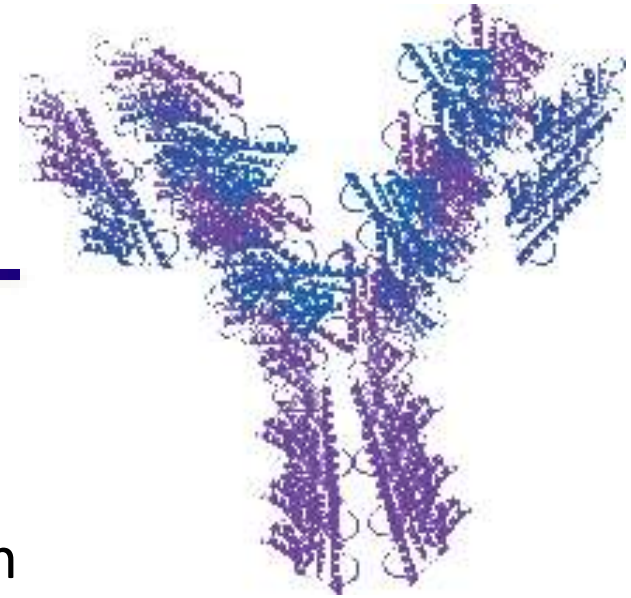


Pancreatic Structure

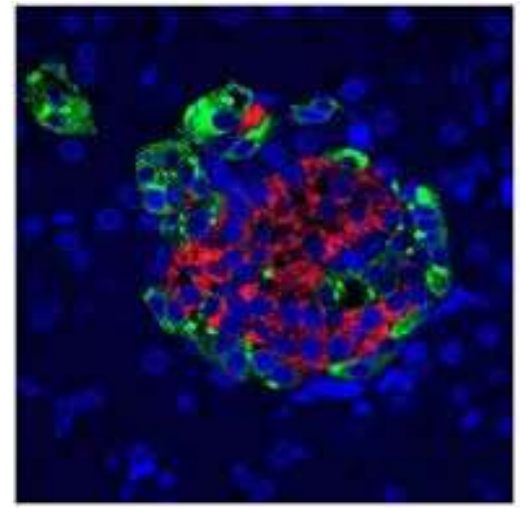


Nature Reviews | Gastroenterology & Hepatology

Pancreatic Polypeptide



- A 36-aa peptide produced by the F (also, γ or gamma) cells of the pancreas, which localize to islets and acinar areas
- PP inhibits secretion of pancreatic enzymes, inhibits contraction of the gallbladder, increases gut motility and gastric emptying
- PP is stimulated by ingested proteins, CCK, secretin, gastrin and vagal input
- Inhibited by somatostatin
- PP modulates insulin receptor expression and availability on hepatocytes. Lack of PP contributes to hepatic insulin resistance
- Overall importance of PP is unclear, but PP is **low in T3cDM**



Types of Diabetes: Comparison

	Type 1 DM	Type 2 DM	Type 3c DM		
	Autoimmune	**Obesity**	**Cystic Fibrosis**	**Chronic pancreatitis**	**Pancreatic resection**
Age at onset	2nd decade	5th- 6th decade	2nd – 3rd decade	5th decade	0-5 years post-op
Exocrine insufficiency	**Up to 5%**	**Up to 30%**	**~100%**	**≤80%**	**≤100%**
Insulin resistance	Unlikely	Yes	No	No	No
Diabetic ketoacidosis	Yes	No	No	No	No
Hypoglycemia risk	Increased	Normal	Normal or increased	Normal or increased	Normal or increased
Pancreatic polypeptide response	Normal or decreased	Normal or increased	Absent	Decreased or absent	Absent

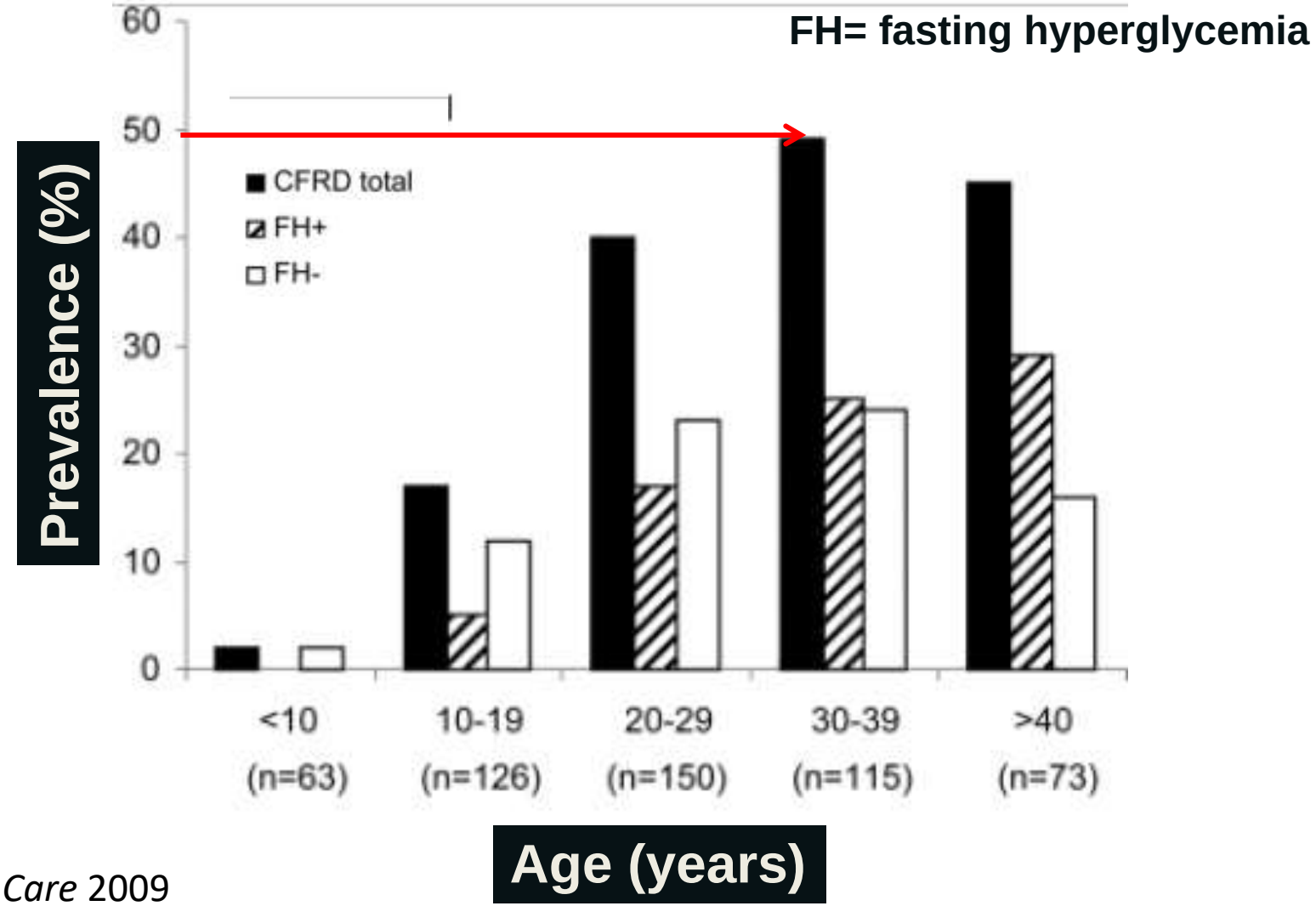
Adapted from: Gudipaty L, Rickels MR. *Pancreapedia,* 2015; Hardt PD, *JOP*, 2008

Pancreatic Exocrine Insufficiency in T1DM, T2DM

- More common than typically recognized, identified by
  - Symptoms of mal-digestion
  - Pancreatic atrophy, fatty infiltration or other changes on imaging
  - Specific testing for PEI often positive
- Contributors:
  - Common pathogenesis, viral, autoimmune, genetic (HNF1β, IPF-1), alcohol or other toxins, pancreatitis
  - Insulin has paracrine trophic effects on acinar cells and structure
  - Islet hormones regulate exocrine tissue, impact exocrine function
  - Diabetic angiopathy or neuropathy

Gudipaty L, Rickels MR. *Pancreapedia,* 2015; Hardt PD in *JOP*, 2008

Cystic fibrosis related diabetes (CFRD) is present in 50% > age 10

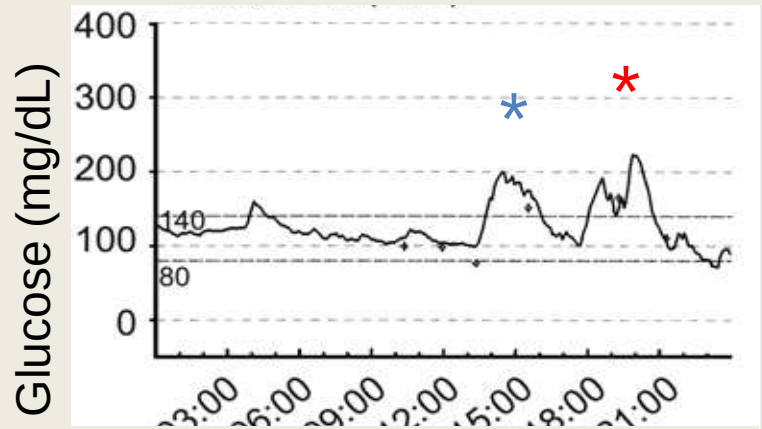


Moran *et al.* *Diabetes Care* 2009

Continuous Glucose Monitoring in CF

NGT (n=22)

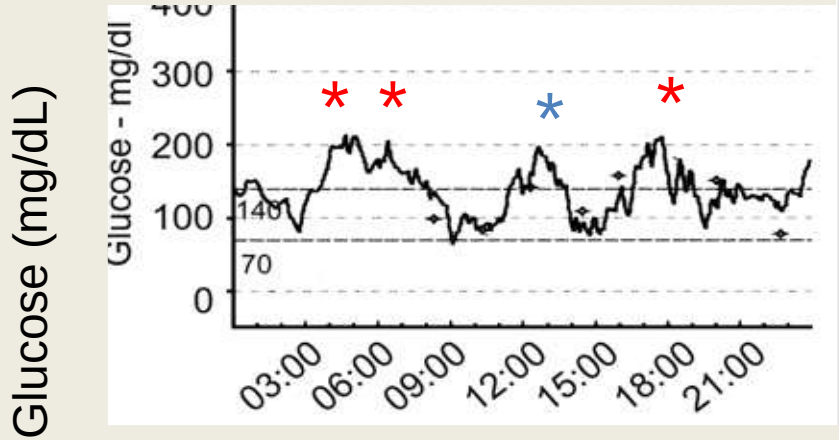
36% at least one glucose **>200 mg/dL**



Insulin secretion defects are evident even in the setting of "NGT"

CFRD (n=10)

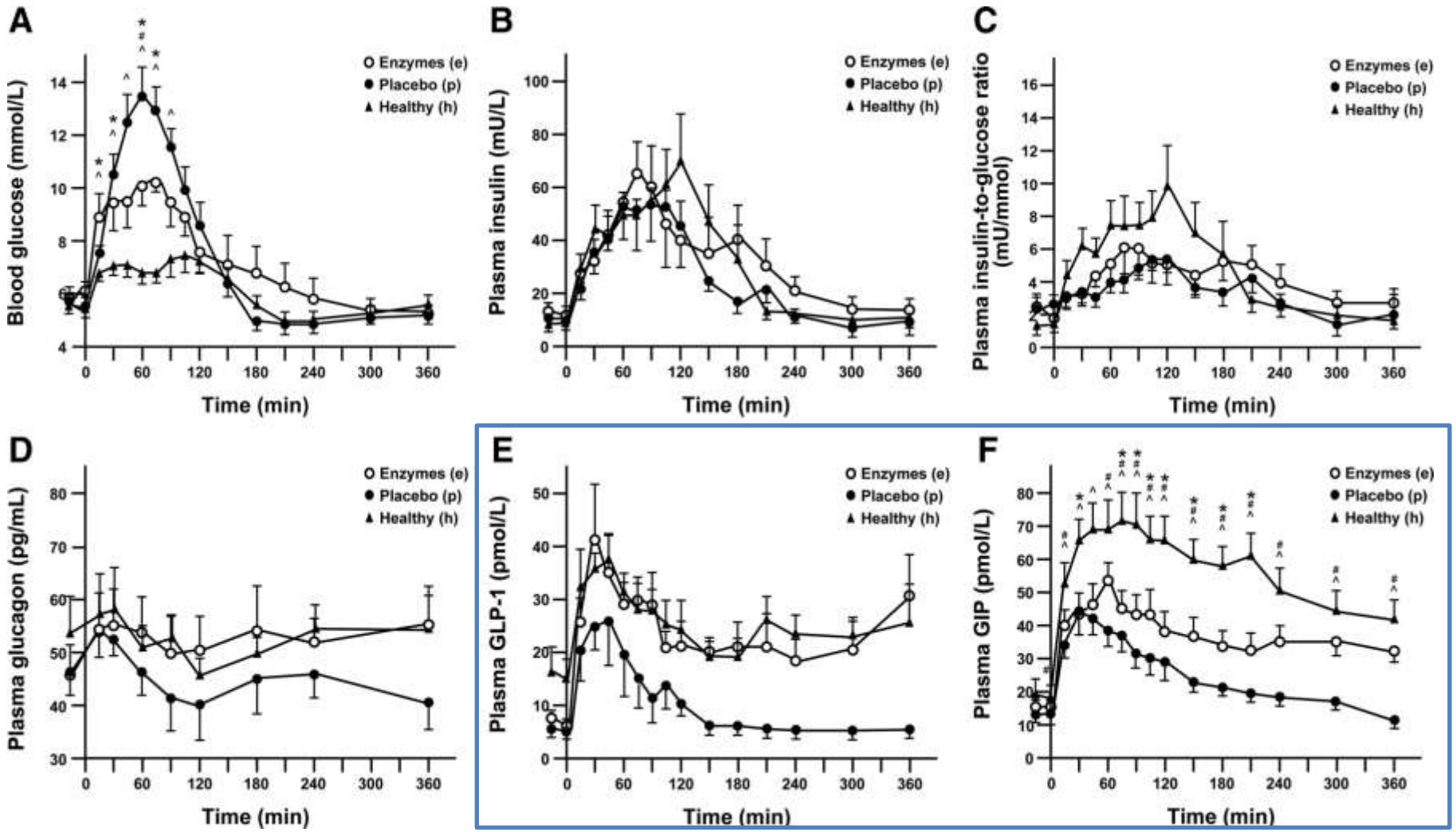
Post meal glucose > 200 mg/dL is common



Moreau et al., *Horm Meta Res,* 2008

Mixed meal tolerance tests in CFRD with and without enzymes

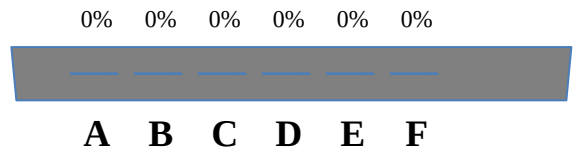
Pancreatic enzymes improve the incretin defect



Kuo P et al, *JCEM* 2011;96:E851-E855

Case 2: Outpatient with Worsening Glucose Control

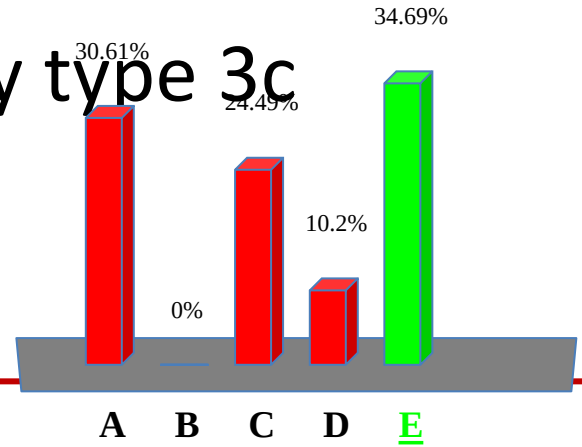
- Pt is a 66 yo woman who had “borderline diabetes for many years, but felt unwell, so she checked her BG, >500 mg/dl. A1c at her PCP office was 11.9%. She was started on metformin and glimepiride and referred to endocrinology.
- Other PMH: CKD, anemia, hypothyroidism, femur fracture from standing. No history of pancreatitis. FH: Diabetes, MI, kidney disease
- With oral medications and dietary efforts, A1c dropped to 9.3% in 4 months.
- Exam was relatively unremarkable, no neuropathy was present.
- Labs: Anti-GAD 0.07 (nl <0.02 nmol/L), C-peptide 5.4 (nl 1.1 – 4.4 ng/mL), sCr 1.85 mg/dL, TSH 8.12 mcIU/mL



Audience Question

What type of diabetes does this patient have?

A. Latent autoimmune diabetes in adults (LADA)
B. Type 2 diabetes
C. Other type of diabetes, possibly type 3c
D. Unable to tell from lab tests
E. Both C & D



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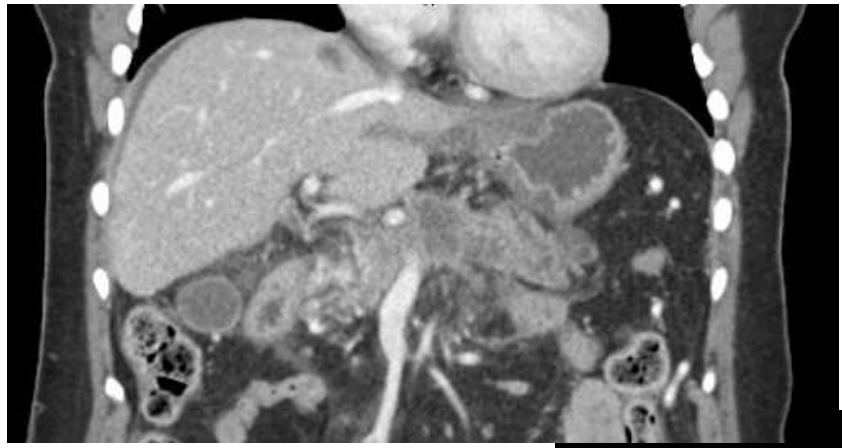
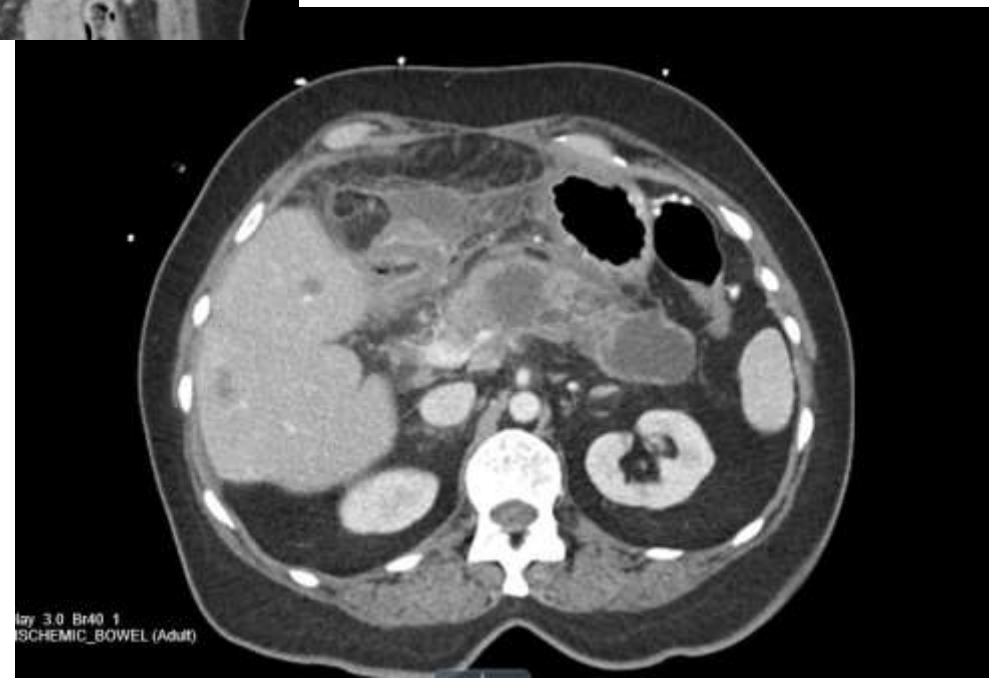
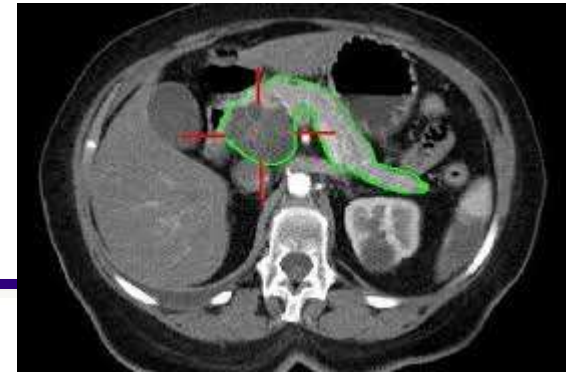
Case 2: Outpatient with Worsening Glucose Control

- CT scan: Lobulated pancreatic mass involving the body and tail of the pancreas extending into the retroperitoneum, encasing the hepatic artery
- Peri-pancreatic stranding suggesting pancreatitis
- Low attenuating lesions in the liver





Worrisome: Pancreatic Cancer Caveats

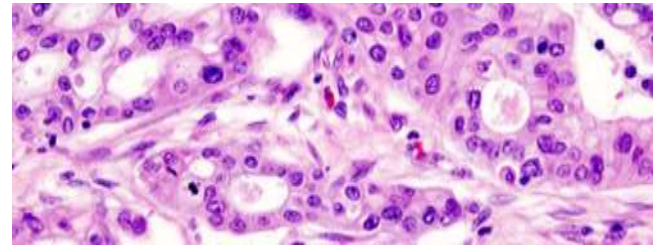


- The prevalence of diabetes in persons with pancreatic disease is > than the population.
- The prevalence of pancreatic disease in persons with diabetes is > than in the population.
- Ask every patient about alcohol intake, known pancreatic disease and family history of pancreatic disease and pancreatic cancer.
- A retrospective review of pancreatic cancer cases at MAYO showed that hyperglycemia was first noted 30-36 months before the tumor was diagnosed.

Chari ST, et. al. Gastroenterology. 2005;129: 504-11, PMID 16083707
Sharma A., et. al. Gastroenterology. 2018;155(2): 490-500

Screening for Pancreatic Cancer

- **USPSTF recommends against routine screening for pancreatic cancer.**
- Individuals with familial pancreatic cancer (2 or more relatives affected with pancreatic cancer, at least 1 first degree relative).
  - 1 first-degree relative, estimated lifetime risk about 6%,
  - 2 first-degree relatives, estimated risk is 8-12%
  - 3 first-degree relatives, estimated risk is 40%



- Germline mutations in ATM (Ataxia telangiectasia syndrome), BRCA1, BRCA2 , CDKN2A, PALB2 (Fanconi Anemia), PRSS1(Hereditary pancreatitis), STK11 (Peutz Jeugers), TP53(Li-Fraumeni Syndrome) and the Lynch syndrome are all associated with pancreatic cancer.

USPSTF task force. JAMA 2019 Aug 6; 322(5): 438-444, PMID 31386141
Lucas AL. JAMA 2019 Aug 6;322(5) 407-8, PMID 31386115

Table 1
Syndromes associated with increased risk of pancreatic cancer

Syndrome	Gene	Estimated Lifetime Risk of Pancreatic Cancer (%)
Peutz-Jeghers syndrome	*STK11*	11–36
FAMMM	*p16/CDKN2A*	10–17
Hereditary breast and ovarian cancer	*BRCA2* *BRCA1*	5 3.6
Fanconi anemia, breast cancer	*PALB2*	Unknown
Lynch syndrome	*MLH1, MSH2, MSH6, PMS2, EPCAM*	3.7
Li-Fraumeni syndrome	*p53*	Unknown
Familial adenomatous polyposis	*APC*	2
Ataxia-telangiectasia	*ATM*	Unknown
Hereditary pancreatitis	*PRSS1*	40
Familial pancreatic cancer	Majority unknown	
1 FDR		6
2 FDR		8–12
≥3 FDR		40

Abbreviations: FAMMM, familial atypical multiple mole and melanoma; FDR, first-degree relative.

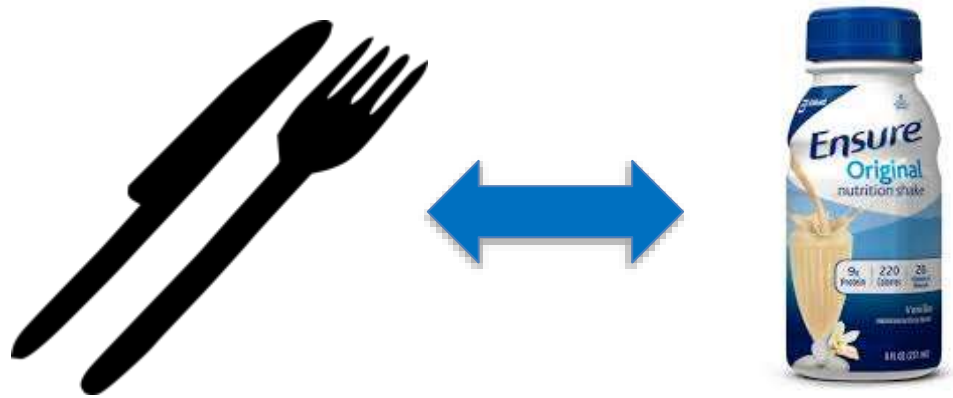
Grover S. et. al. Gastroenterol Clin N Am 45(2016) 117-127; http://doi.org/10.16/j.gtc2015 10.001

Type 3c Diabetes Patient assessment

Iron Profile,
Sweat chloride,
Genetic
testing?

Nutrition in Pancreatic Disease: It's Complicated

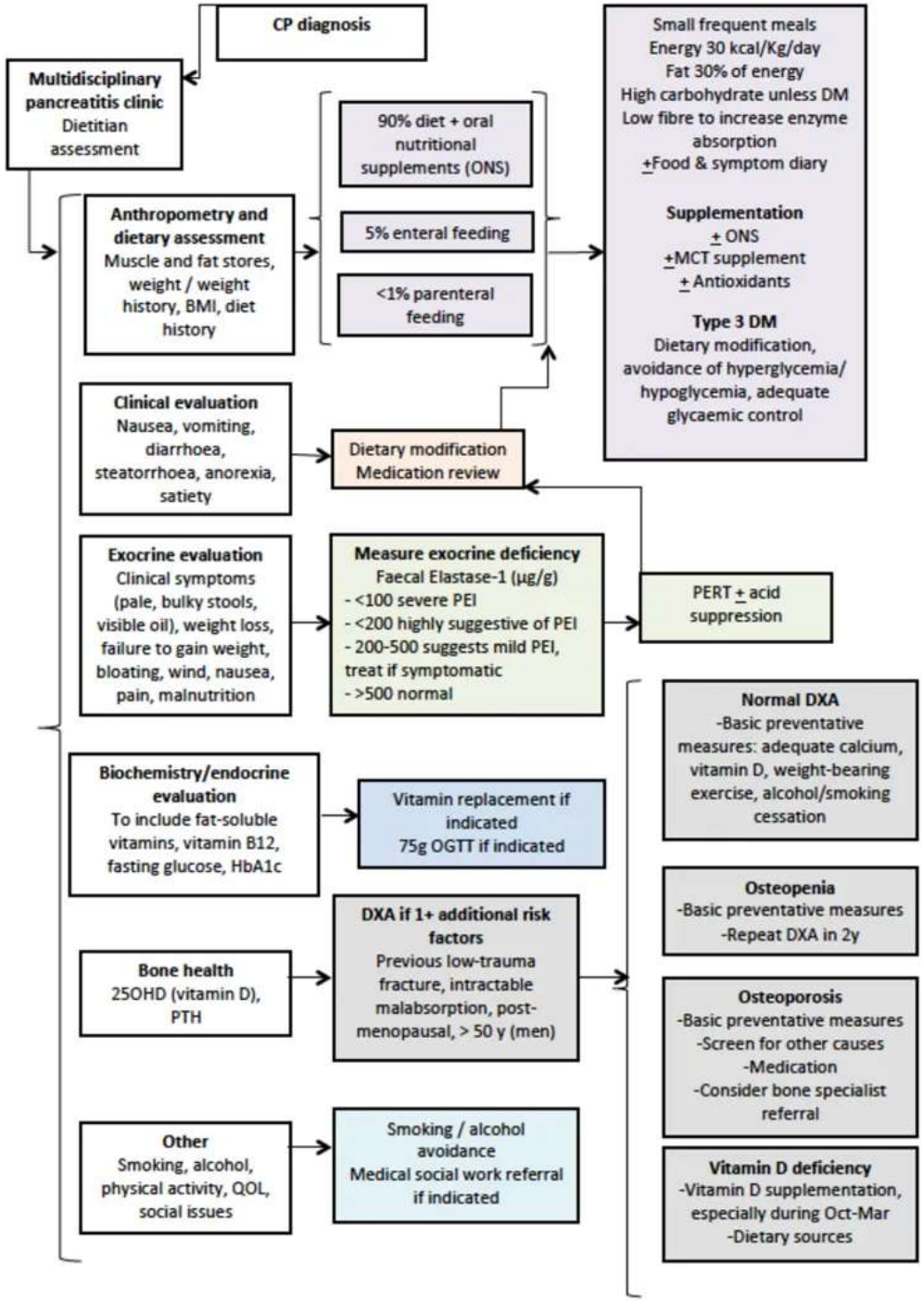
- Protein-calorie malnutrition is common
- Low fat, low fiber, lower density – recommendations are individualized
- Vitamin deficiencies (A,D,E,K), may require supplements
- Other deficiencies (iron, Zn, B-vitamins, vitamin C, omega 3 fatty acids)
- Need for enzyme replacement
  - Timing/dose of enzyme replacements, exactly with food, snacks and supplements
- Dietary supplements (required by 10 – 15%)
  - Elemental
  - Clear, many others
- Enteral feeding (5%)
  - Nighttime nasal vs J-G tube feeds
- Parenteral feeding (rare)



O'Brien SJ, *Nutr in Clin Practice, 2019*

Nutrition Therapy in PEI and Type 3c Diabetes

- Multidisciplinary approach
- Assessment if exocrine and endocrine dysfunction
- Ongoing modification based on symptoms and nutrition status
- Use of acid reducers, pancreatic enzyme replacement therapy (PERT), oral nutrition supplements, vitamin supplements.
- Bone health evaluation
- Stop alcohol and smoking!



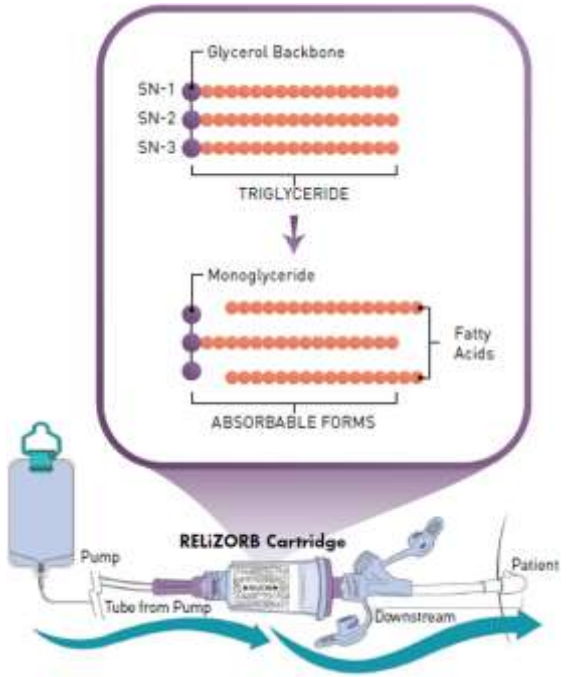
Duggan S, *Nutr Clin Pract,* 2010; Duggan S et al, *Eur J Clin Nutr,* 2017

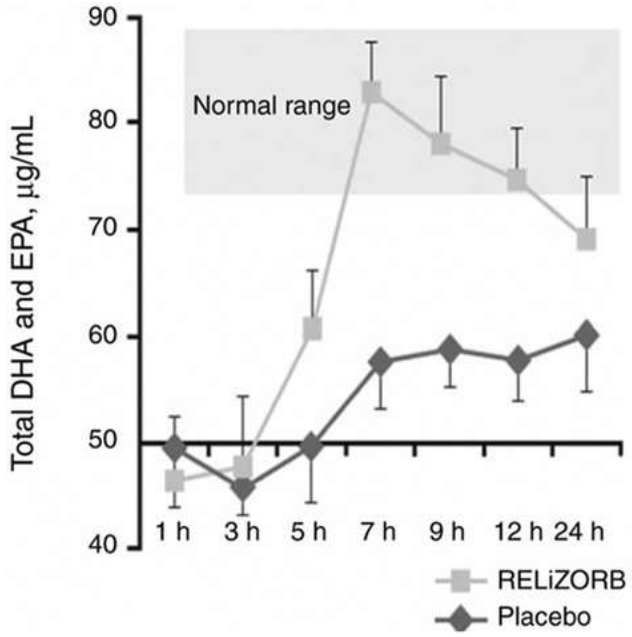
Case in Point: CFRD Nutrition Recommendations

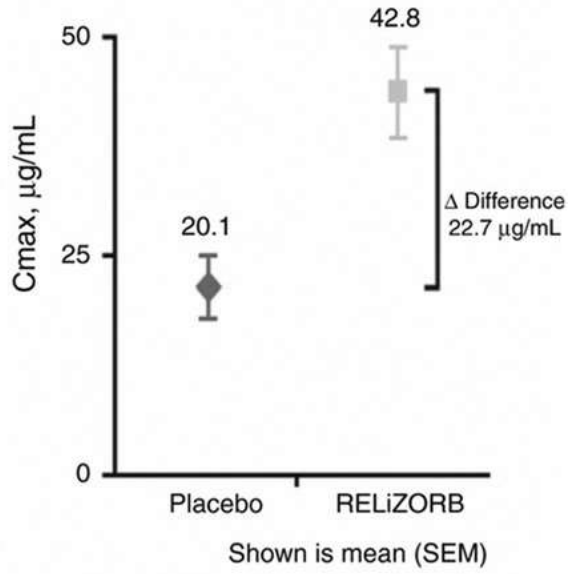
- Caloric needs are high due to increased work of breathing, inflammation, malabsorption and growth
- Pancreatic enzyme replacement should start in childhood, prior to onset of diabetes
- Calorie distribution: 45 – 50% fat, 15% protein, 35-40% carbs
- Supplementation:
  - Fat soluble vitamins A, D, E, K
  - Omega 3 fatty acids
  - Sodium, follow FENa to assure adequacy
  - Other nutrients: iron, Zn, B-vitamins, vitamin C, Calcium

Slae M, *Curr Opinion Pulm Med*, 2019

Lipase Cartridge Added to Tube Feeds







Use of lipase cartridge in the tube feed line breaks down triglycerides to monoglycerides and fatty acids, improves essential fatty acid levels.

O'Brien SJ, *Nutr in Clin Practice, 2019;* Freedman S, *J Ped Gastroenterol Nutr,* 2017

Glucose Monitoring in Patients with T3cDM

- Goals of therapy
  - Glycemic control to protect from microvascular complications
  - Avoidance of hypoglycemia
  - Understanding interactions between diet, enzymes and insulin needs
- SMBG with glucose meters
  - Need to check fasting and post-prandial to understand this disease
- Continuous Glucose Monitoring
  - Real-time, more accurate in hypoglycemic ranges
  - Intermittent, more cost effective
- HbA1c may be less accurate if anemia is present, iron and zinc deficiency, other serious illnesses

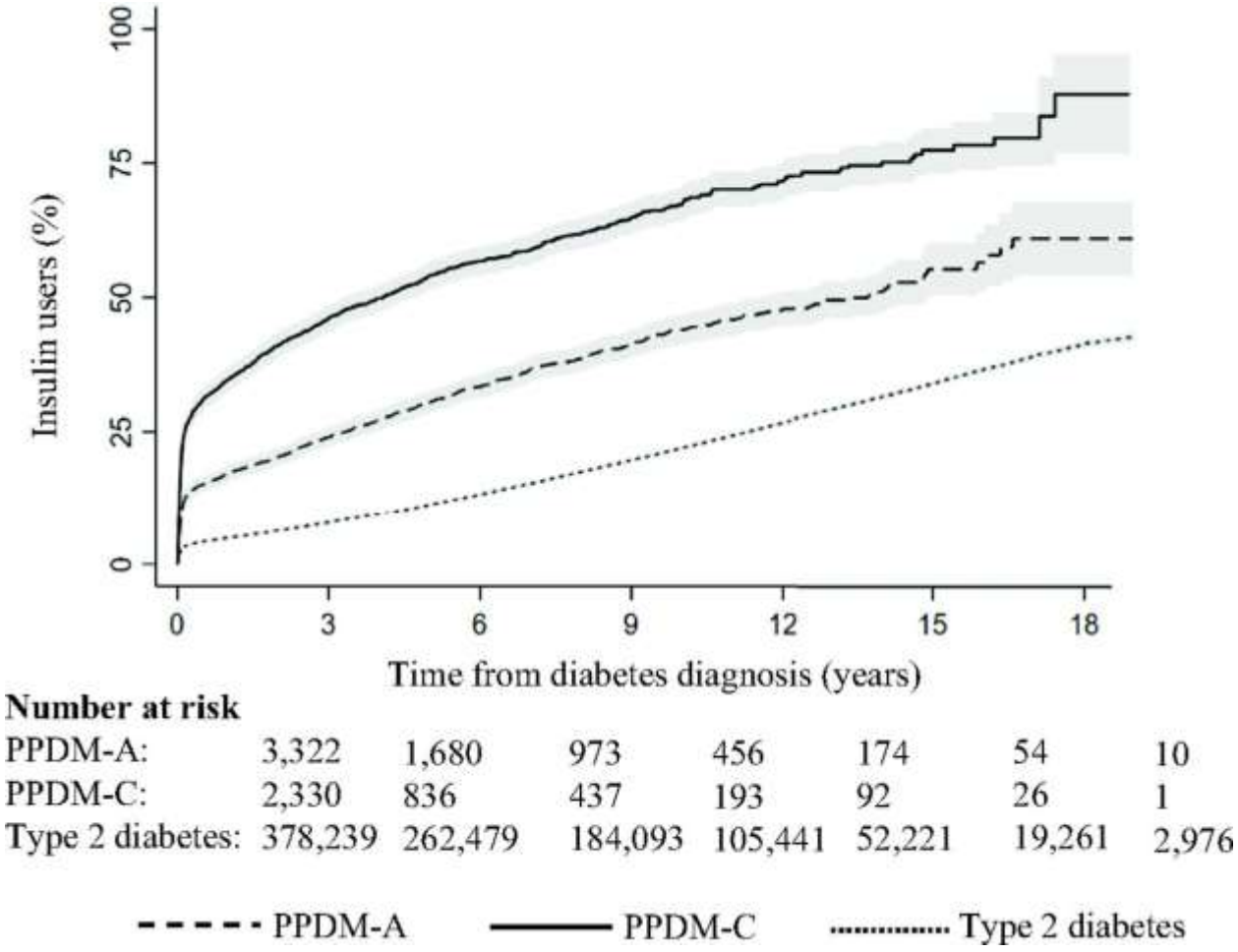
Diabetes Management in Patients with T3cDM

- Major problem:
  - Increased risk for treatment related hypoglycemia.
  - Low basal insulin requirement due to low muscle mass
  - Lower risk for DKA due to the absence of glucagon
- Non-insulin treatment may work initially
  - Metformin is OK
  - Avoid DPP4 inhibitors, GLP1 receptor agonists; avoid SGLT2 inhibitors
- Insulin dosing
  - Give basal insulin in the am to decrease the risk of hypoglycemia overnight. Basal dosing 0.1-0.15 units per kg.
  - Mealtime insulin is needed, variable doses, timing with intake + enzymes
- Encourage use of pancreatic enzymes at all meals and snacks if PEI or nutritional deficiencies are demonstrated

Progressive Diabetes, Insulin Deficiency Common in Type 3c Diabetes

Diabetes after acute or chronic pancreatitis is progressive

- Early insulin needed by some
- GLP1-RA, DPP4i, SFU used (but not indicated)
- At 12 years, 75% of chronic pancreatitis patients, and 50% of those with a single acute pancreatitis episode require insulin



Viggers R, Diabetes Care, 2020

Management of T3c Diabetes

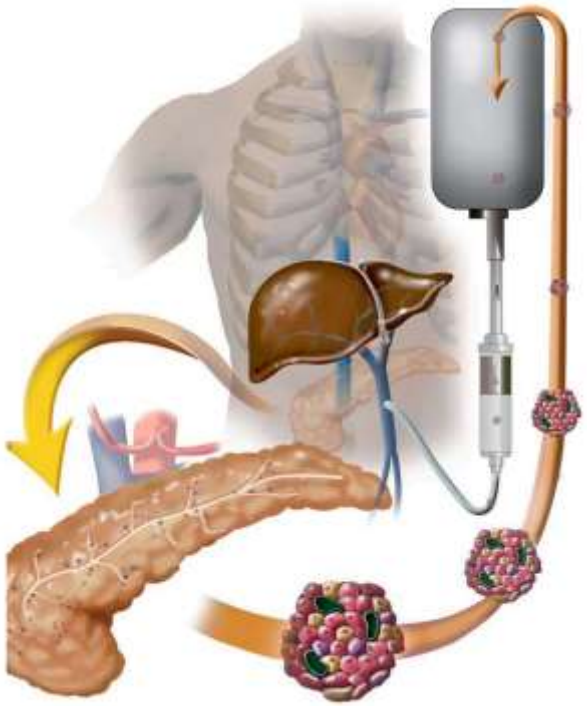
Nutrition Concerns

- Adequate macronutrients
- High fat intake recommended for CF, ? Appropriated for non – CF PEI?
- Timing/food intake distribution (multiple small meals vs larger meals)
- Risk of hypoglycemia suggests that time between meals should be shortened, ie frequent feedings
- Re-inforce the need for pancreatic enzymes; titrate the dose based on steatorrhea and symptoms

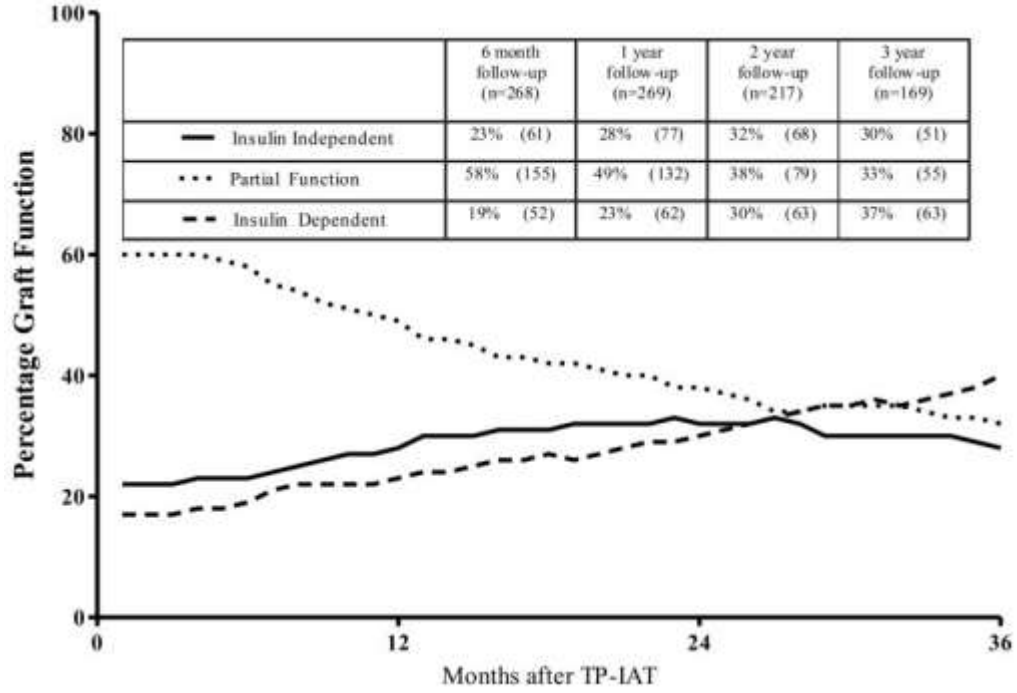
Diabetes Treatment

- High calorie meals may require higher meal-time insulin than expected
- Multiple small meals – treat with multiple doses of rapid acting insulin or R
- Consider insulin pump if resources allow, makes frequent insulin dosing possible
- CGM is a great help to prevent hypoglycemia, especially real-time CGM with alarms

Total Pancreatectomy with Islet Auto-Transplantation



	6 month follow-up (n=268)	1 year follow-up (n=269)	2 year follow-up (n=217)	3 year follow-up (n=169)
Insulin Independent	23% (61)	28% (77)	32% (68)	30% (51)
Partial Function	58% (155)	49% (132)	38% (79)	33% (55)
Insulin Dependent	19% (52)	23% (62)	30% (63)	37% (63)



At 3 years, 90% have some β-cell function, 1/3 are insulin independent, 2/3 require some or full insulin replacement

Google Images, Penn Medicine and Sutherland D, *J Am Coll Surgery,* 2013

Treatment of Pancreatic Diabetes: Tailored nutrition therapy +/- pancreatic enzymes

Use of CGM to reduce the risk of hypoglycemia;
treat hypoglycemia with pure glucose only

Total Pancreatectomy with Islet Autotransplantation, Nutrition/Insulin/Enzymes

MDI Insulin Regimen Enzymes/Supplements/Enteral Support/Vitamins

Metformin + Insulin Nutrition Counseling/Supplements Vitamins/Enzymes

Metformin only Vitamin Replacement if needed

Early treatment, monitor HbA1c, fasting and post-prandial glucoses

Avoid GLP1 receptor agonists, DPP4 inhibitors, sulfonylureas

Summary: What have we learned?

- Type 3cDM is common and is often misdiagnosed
- Characterization of pancreatic function (stool tests, vitamin levels, imaging) may be necessary for the diagnosis and to plan treatment
- Determine the etiology of the pancreatic dysfunction and assess the risk of pancreatic cancer
- Assess caloric needs and macronutrient distribution
- Metformin in mild cases, but most will need pre-meal insulin; advanced cases or post-pancreatectomy will need basal-bolus
- Follow-up should include weight, height, vitamin and mineral levels, symptoms, and glycemic parameters


thank
you!