INTRODUCTION TO DIABETES

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2/3/2024

2024 Virtual Diabetes Management Conference for School Nurses

Provided by Texas Children's Hospital

NURSING CONTINUING PROFESSIONAL DEVELOPMENT

Texas Children's Hospital is approved with distinction as a provider of nursing continuing professional development (NCPD) by the Texas Nurses Association, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

REQUIREMENTS FOR SUCCESSFUL COMPLETION

To receive contact hours for this nursing continuing professional development activity, the participant must:

- Register for the continuing professional development activity
- Attend at least one session of the professional development activity
- Complete the pre-conference survey
- Complete the post-conference survey online

Print your contact hour "Certificate of Successful Completion" once you have completed the post-conference survey online .

LEARNING OUTCOME

As a result of this professional development activity, 90 % of attendees will be able to name one concept learned on the post conference survey as it relates to care of the child with diabetes as well as attendees will demonstrate increased knowledge as evidenced by an increase in scores on the post conference survey when compared to the pre-conference survey.

RELEVANT FINANCIAL RELATIONSHIPS

Explanation: a relevant financial relationships occurs when an individual has an opportunity to affect or impact educational content with which he or she may have a relationship with an ineligible company or a potentially biasing relationship of a financial nature. All planners and presenters/authors/content reviewers must disclose the presence or absence of a relevant financial relationship relative to this activity. All potential relationships are mitigated prior to the planning, implementation, or evaluation of the continuing education activity. All activity planning committee members and presenters/authors/content reviewers have had their relevant financial relationships assessed, identified and mitigated by Activity Director & the nurse planner.

The activity's Nurse Planner has determined that no one who has the ability to control the content of this nursing continuing professional development activity – planning committee members and presenters/authors/content reviewers – has a relevant financial relationship.

DISCLOSURE

- I have no relevant financial relationships with any ineligible company to disclose.

- I do not intend to discuss unlabeled or unapproved use of drugs or products in this presentation.

OBJECTIVES

1. Describe the estimated prevalence of Type 1 and Type 2 Diabetes
2. Discuss the pathophysiology of Type 1 vs Type 2 Diabetes
3. Review presenting symptoms of diabetes
4. Discuss the diagnostic criteria for diabetes
5. Briefly review the management of diabetes

CONTENTS

- **Incidence and Prevalence**
- Etiology and Pathogenesis
- Signs/Symptoms
- Diagnostic Criteria
- Management

INCIDENCE OF DIABETES

- One of the most common chronic diseases in the school-aged child
- Affects >190,000 (~1 out of 465) youth aged <20 years
  - 45% relative increase in T1D over 16 years from 2001-2017
- Factors: Age, race/ethnicity, geography, secular changes, seasonality

Geographical Variations in T1D Incidence

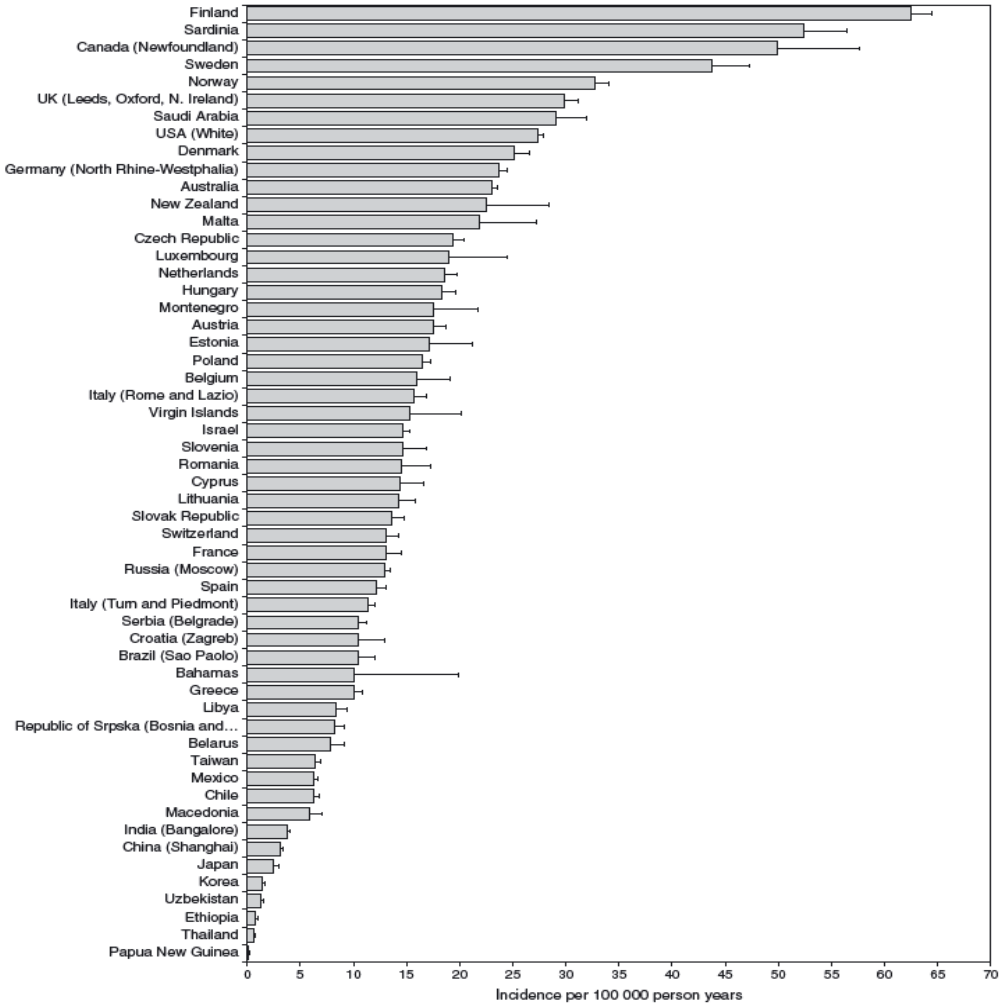

Fig. 1. Global mean annual incidence rates of type 1 diabetes in children and adolescents aged 0–14 yr. Only countries in which the study period included data from 2000 onwards are shown [adapted from the International Federation atlas (39)].

PREVALENCE OF T1D AND T2D DIABETES IN YOUTH

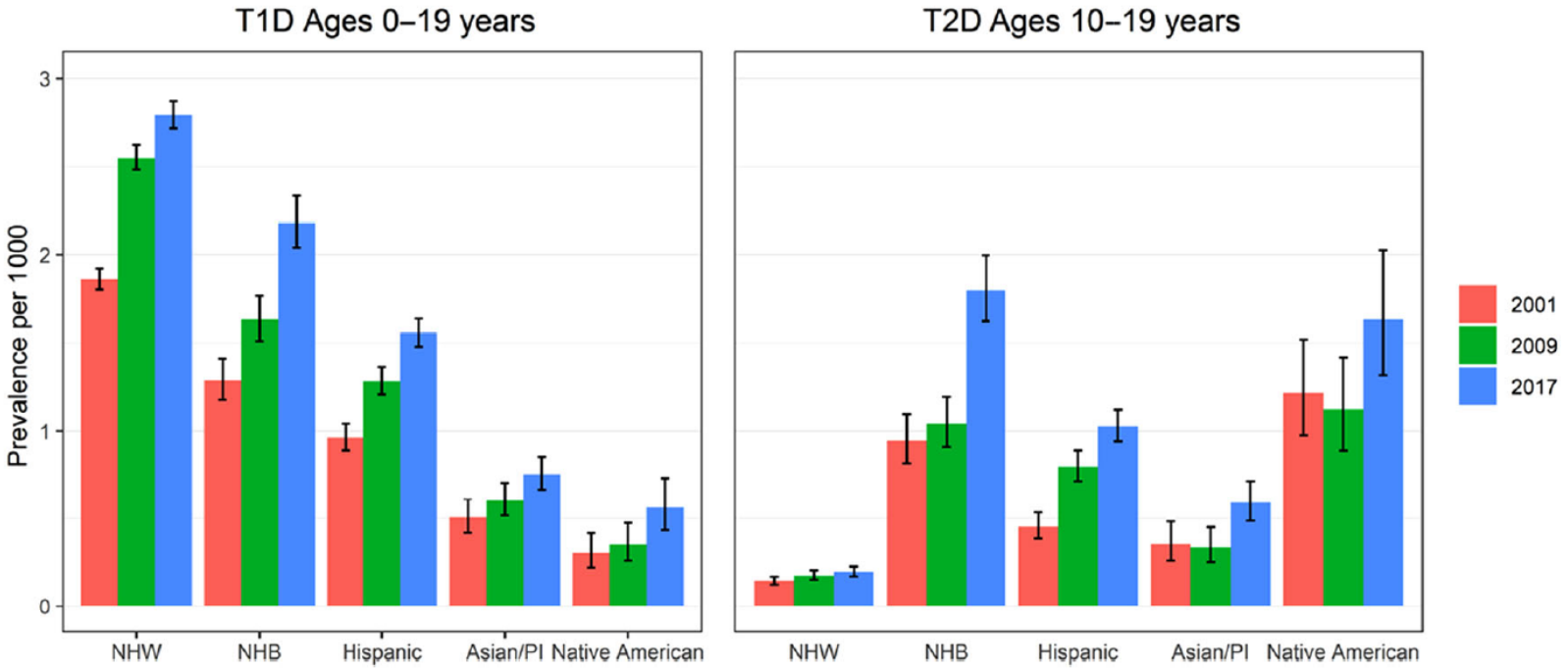

Figure 4. Prevalence per 1000 youth <20 years of age at onset by type (T1D and T2D) by race/ethnicity and year (2001, 2009, and 2017).[14] Significant increases ($P < 0.05$) in T1D and T2D were observed from 2001 to 2017 for each race/ethnicity group, except for T2D among Native Americans ($P = 0.06$). The greatest increases in T1D were among NHW and NHB and for T2D, among NHB, Hispanics, and Asian/PIs. Asian/PI, Asian Pacific Islander; NHB, non-Hispanic Black; NHW, non-Hispanic White.

Dabelea et al. *Twenty Years of Pediatric Diabetes Surveillance: What Do We Know and Why It Matters.* Annals of the New York Academy of Sciences 2021;PMID: 33543783.

PREVALENCE OF TYPE 2 DIABETES

Rising prevalence occurring parallel with increasing prevalence of Obesity

- 1990s – T2DM represented ~ 3% of Pediatric Diabetes
- 2003 – T2DM represented ~ 20% of pediatric diabetes
- Increase in prevalence by 30.5% in youth between 2001 and 2009 (SEARCH study)
- 95.3% relative increase in prevalence in youth between 2001-2017

CONTENTS

- Incidence and Prevalence
- **Etiology and Pathogenesis – Type 1 Diabetes**
- Signs/Symptoms
- Diagnostic Criteria
- Management

Type 1 Diabetes – immune-mediated β-cell destruction, leading to insulin deficiency and lifelong insulin requirement

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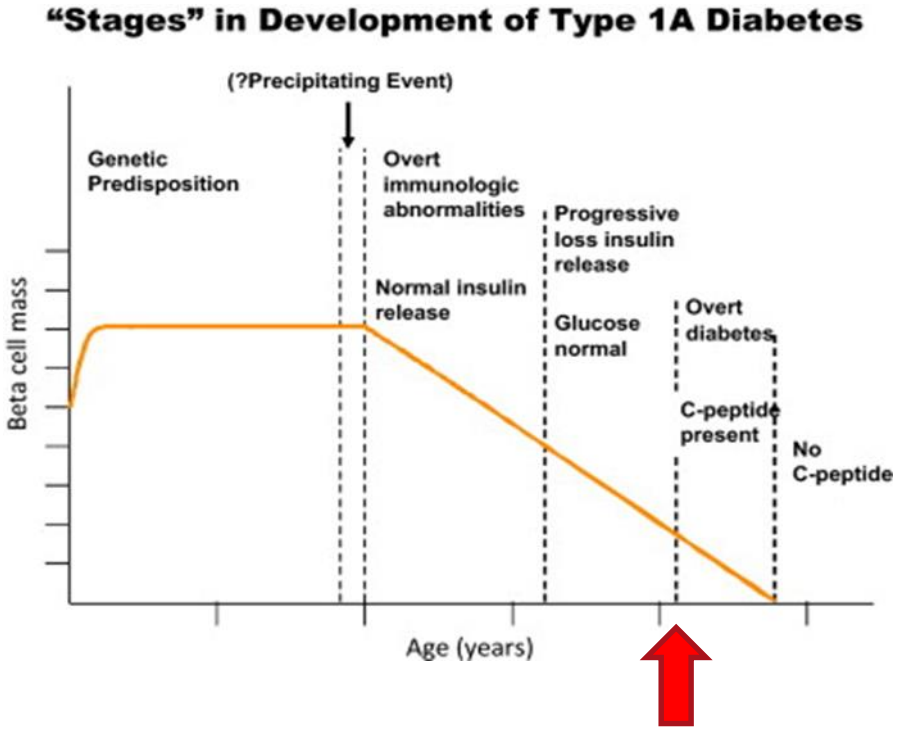
EISENBARTH MODEL OF STAGES IN T1D DEVELOPMENT



G.S. Eisenbarth NEJM 1986

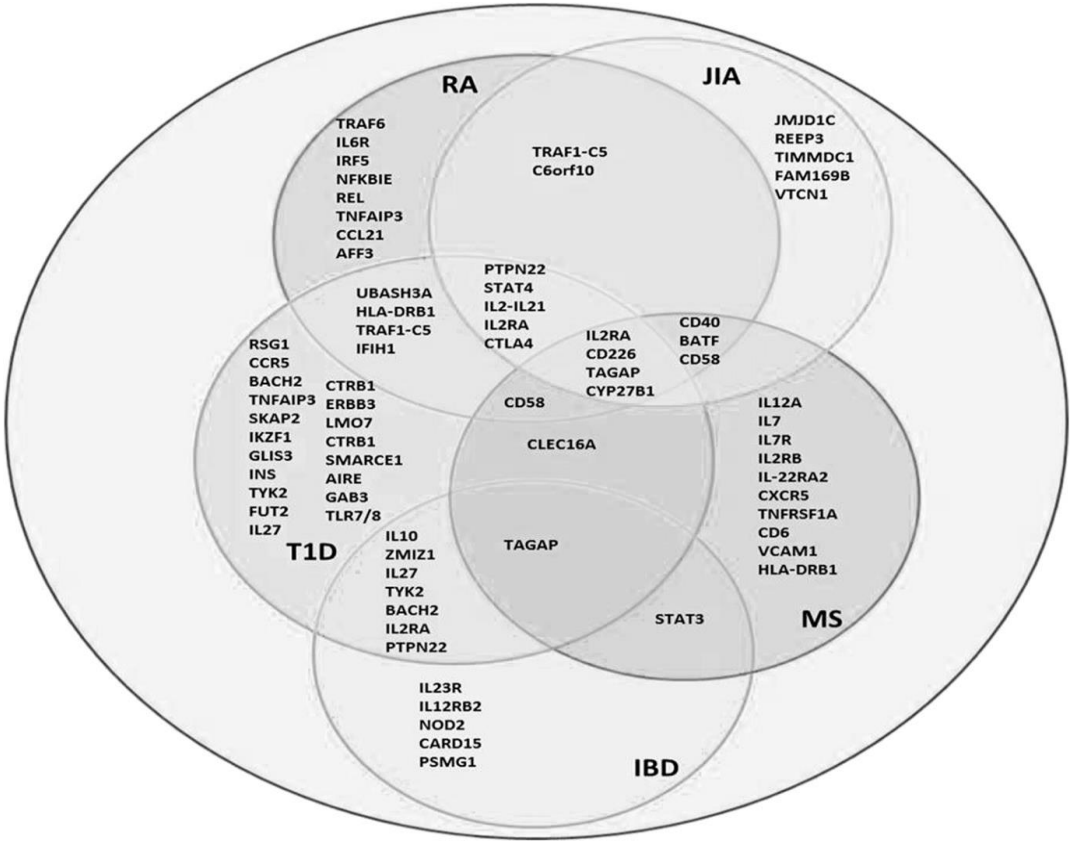
FAMILIAL AGGREGATION

- General population: 0.4%
- Siblings of patients: 6%
- Children of male patient: 6-9%
- Children of female patient: 1.3-4%
- Monozygotic twins of patients: 50-70%

GENETIC FACTORS INVOLVED IN T1D

- HLA Haplotypes
- Insulin Gene
- PTPN22
- Cytotoxic T-lymphocyte associated protein 4 (CTLA-4)
- Interleukin-2 receptor subunit alpha (IL2RA)
- Protein tyrosine phosphatase, non-receptor type 2 (PTPN2)
- Interferon-induced helicase (IFH1)
- Small ubiquitin-like modifier 4 protein (SUMO4)
- Basic leucine zipper transcription factor 2 (BACH2)

GENETIC BASIS OF ASSOCIATION WITH OTHER AUTOIMMUNE DISEASES



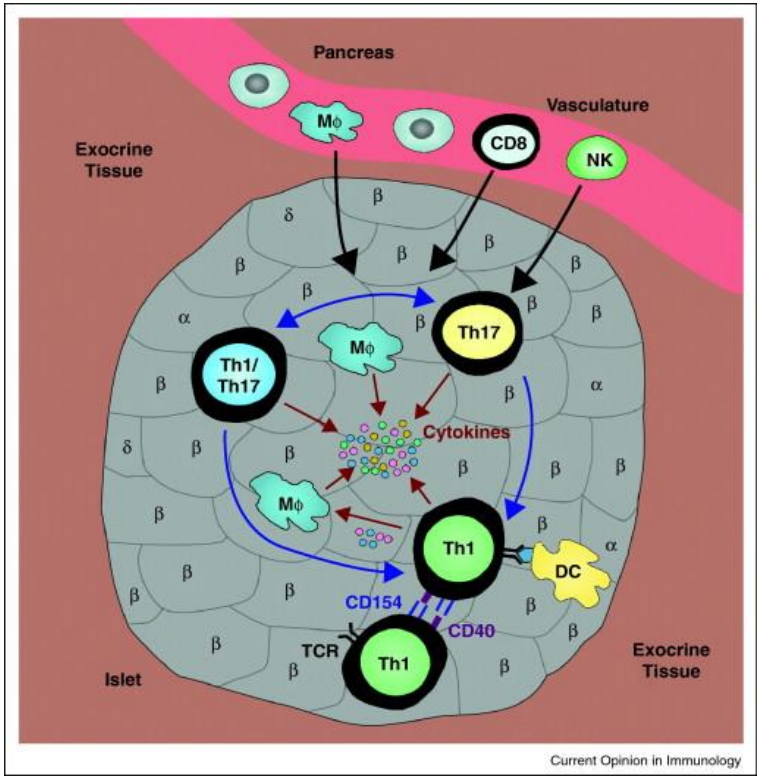
CHALLENGES

- Complex genetic effects
  - Imprinting (insulin gene)
- Acquired genetic polymorphisms (e.g. by retrovirus)
- Epigenetics
- Gene-gene interactions
- Interaction between genes and environment (e.g. genes related to vitamin D metabolism)
- Studies on non-Caucasian ethnic groups
- Heterogeneity of T1D

ENVIRONMENTAL FACTORS

- Viruses
- Cow's milk v breastfeeding:
- Diet, bacteria
- Vitamin D
- Effect of obesity/overweight
- Hygiene hypothesis
- Vaccines: No!

PATHOGENESIS OF TYPE 1 DIABETES



- Auto-reactive T cells
- Insulitis
- Beta-cell death

Haskins et al. Current Opinion in Immunology, 2011

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MEASURES OF BETA-CELL FUNCTION LOSS

Beta-cell dysfunction:

↓ Beta-cell glucose sensitivity

↓ Insulin-to-proinsulin ratio

↓ First phase of insulin secretion

↓ Insulin and C-peptide secretion

Metabolic abnormality:

↑ HbA1c

↑ Postprandial glucose

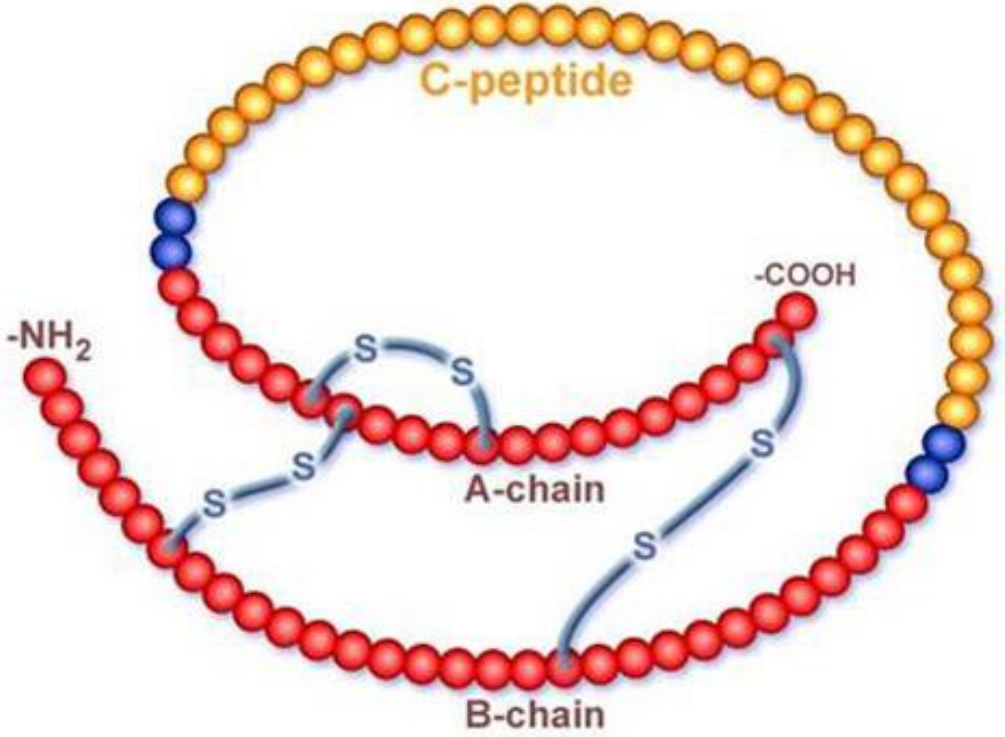
↑ Fasting glucose

Clinical correlates:

↑ Exogenous insulin requirements

Diabetic ketoacidosis

C-PEPTIDE IS CO-SECRETED WITH INSULIN



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ANTI-ISLET AUTOANTIBODIES (AAB)

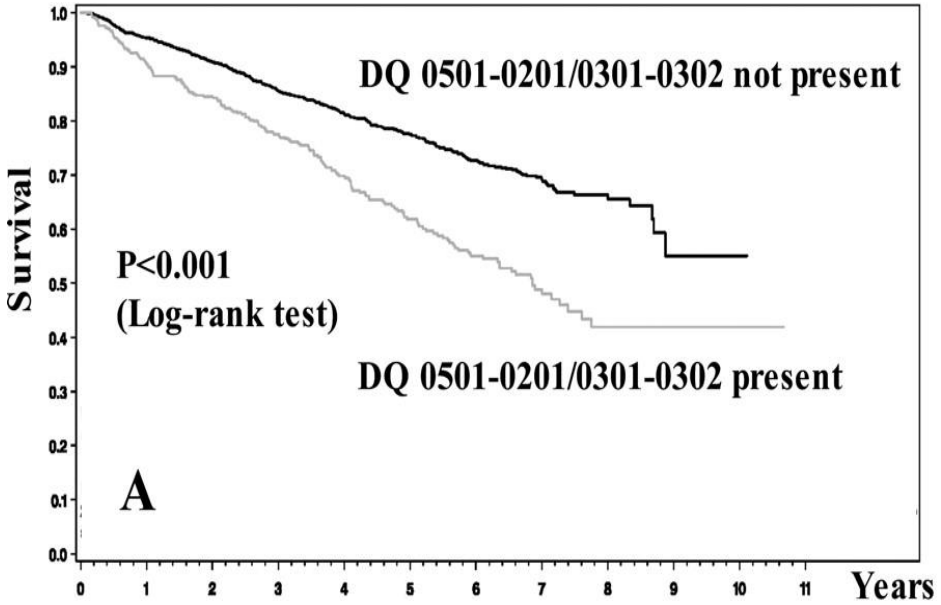
- Markers (not causative) of beta-cell destruction
  - Diagnosis
  - Prediction
- >=1 expressed in 90-95% of T1D cases
  - Islet cell antibody (ICA)
  - Biochemical:
    - Insulin (IAA)
    - Glutamic acid decarboxylase (GAD65)
    - Thyroxine phosphatase-like protein (ICA512/IA-2)
    - Zinc transporter (ZnT8-Arg and –Trp)

ANTI-ISLET AUTOANTIBODIES PREDICT T1D

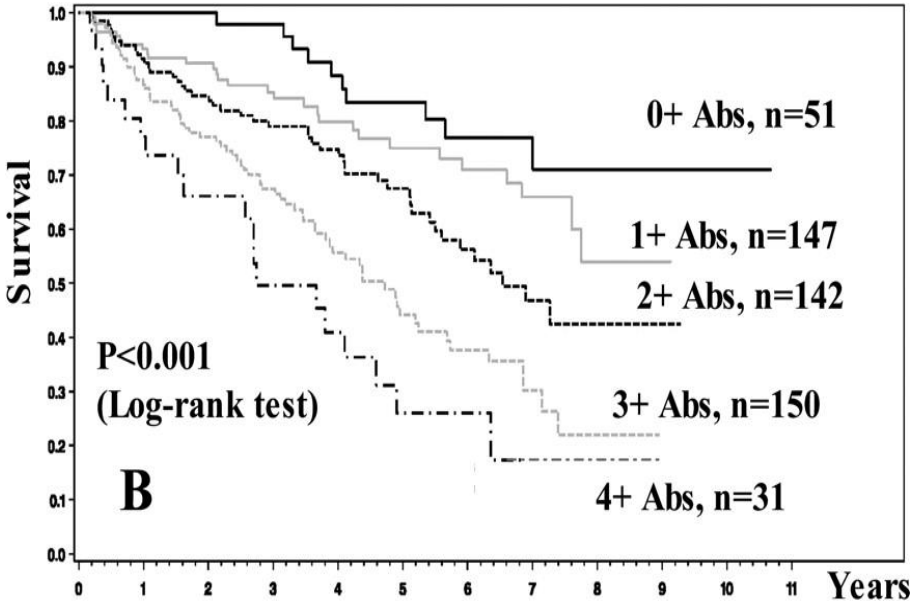
- Appear even years before diagnosis
- Higher T1D risk with:
  - Higher number positive:
    - >=2 positive: 70% T1D risk in 7 yrs
  - Higher titer
  - Certain specificities and combinations
  - Genetic background:
    - Monozygotic twins
    - Relatives
    - T1D-associated HLA haplotypes

PROGRESSION TO T1D IN RELATIVES OF PATIENTS

Higher risk in DQ2/DQ8 relatives

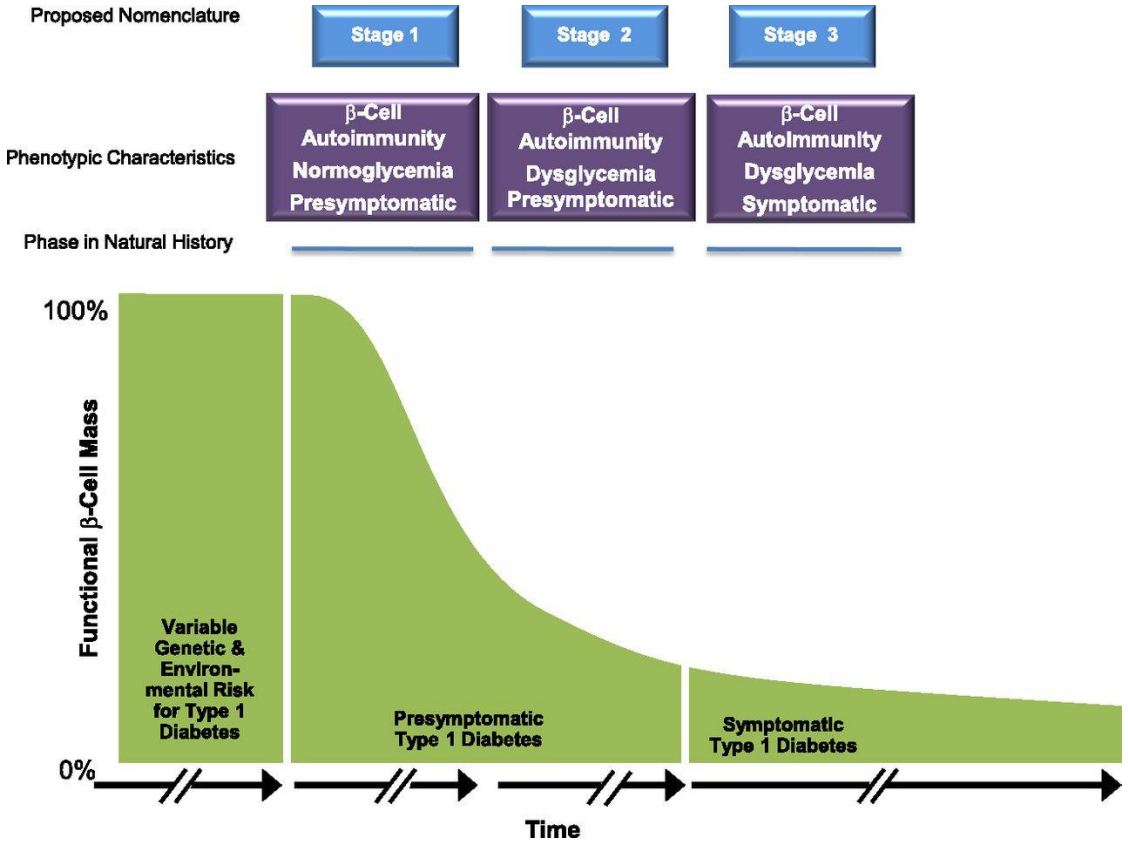


Highest risk in DQ2/DQ8 relatives with multiple +Aabs



Redondo M J et al. J Clin Endocrinol Metab 2006;91:1705-1713

EARLY STAGES OF TYPE 1 DIABETES



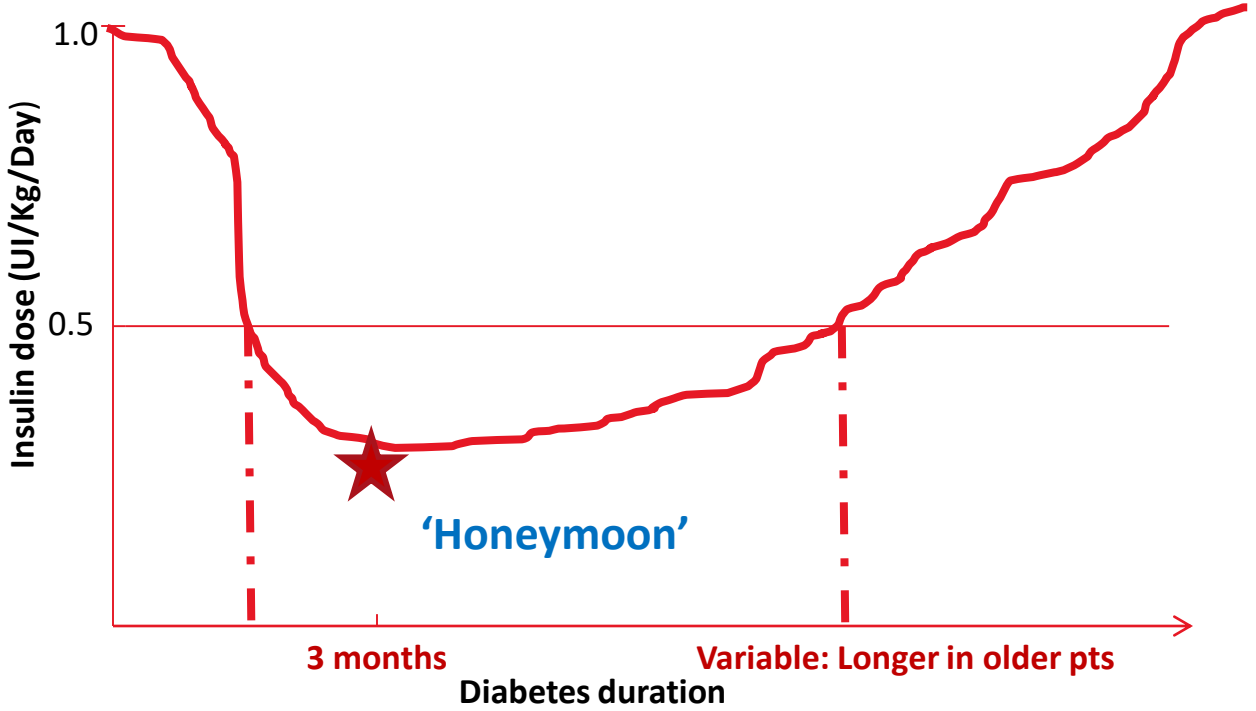
Richard A. Insel et al. Dia Care 2015;38:1964-1974

The Endocrine Society

JDRF Improving Lives. Curing Type 1 Diabetes.

American Diabetes Association.

EXOGENOUS INSULIN REQUIREMENTS AFTER T1D ONSET



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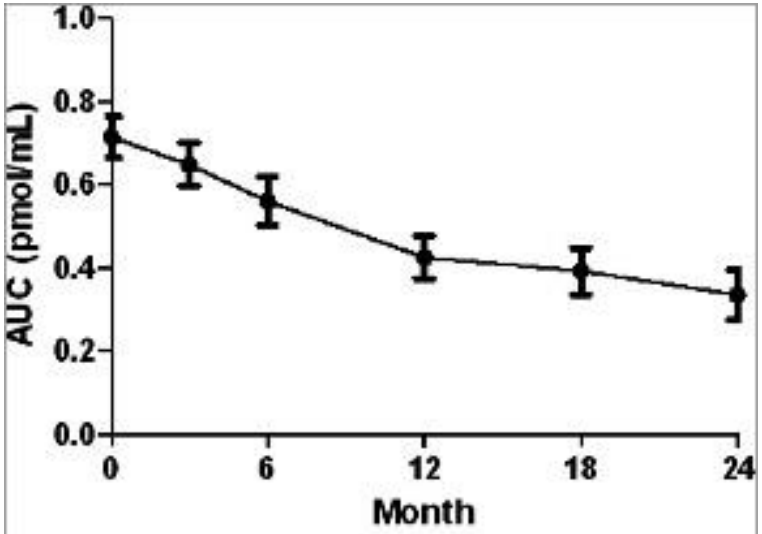
PARTIAL REMISSION PERIOD ('HONEYMOON')

- **Definition:**
  - Temporary partial beta-cell functionality after initiation of therapy (Glucotoxicity resolving?)
  - Total daily insulin (TDI)<0.5 U/kg/day; TDI-adjusted A1c<9%
- **Benefits of "honeymoon":**
  - Easier to treat diabetes:
    - Better Hb1c
    - Lower postprandial hyperglycemia
    - Less hypoglycemia
  - Predicts less long-term chronic complications

C-PEPTIDE DECLINE AFTER ONSET



Month	Standard Deviation
0	0.34
3	0.35
6	0.39
12	0.34
18	0.37
24	0.37

Greenbaum et al. Diabetes 2012

CONTENTS

- Incidence and Prevalence
- **Etiology/Pathogenesis – Type 2 Diabetes**
- Signs/Symptoms
- Diagnostic Criteria
- Management

Type 2 Diabetes – insulin resistance with failure of β-cell compensation and a relative insulin deficiency

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RISK FACTORS FOR CHILDHOOD-ONSET T2DM

- Obesity
- Positive Family history
- Specific racial and ethnic groups
- Female gender
- Conditions associated with insulin resistance

CONTENTS

- Incidence and Prevalence
- Etiology/Pathogenesis
- **Signs/Symptoms of Diabetes (Type 1 and Type 2)**
- Diagnostic Criteria
- Management

CLINICAL PRESENTATION

- Polyuria, polydipsia, and weight loss with dehydration
- ~40% are in clinically apparent DKA (diabetic ketoacidosis)
  - Occasionally children with T2DM can present with DKA (~6% frequency for initial presentation)

ACANTHOSIS NIGRICANS

- Clinical sign of insulin resistance
- Dark, velvety patches on skin folds and creases
- Increased risk to develop Type 2 Diabetes

LABORATORY EVALUATION

- Elevated serum glucose – fasting >126, random >200
- Glycosuria – renal threshold 185 mg/dl
- Blood or urine ketone bodies
- Pseudo-hyponatremia
- Elevated triglycerides
- Hemoglobin A1C

DKA PRESENTATION

- Initial presenting signs: polyuria, polydipsia, weight loss, dehydration, abdominal pain, Kussmaul respirations
- Labs:
  - **(D)** Hyperglycemia – glucose > 200
  - **(K)** Ketosis – ketones in serum or urine
  - **(A)** Acidosis – pH <7.3, bicarbonate < 15
  - Other labs can include: pseudohyponatremia, elevated WBC (infection), elevated BUN (dehydration), any level potassium

TREATMENT OF DKA

- Measure labs and establish diagnosis
- Fluid and Electrolyte Replacement
- IV Insulin Therapy
- Monitoring

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- Incidence and Prevalence
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- Signs/Symptoms
- **Diagnostic Criteria**
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DIAGNOSTIC CRITERIA FOR DIABETES

- A1C ≥6.5%

OR

- Fasting plasma glucose ≥ 126 mg/dl

OR

- 2 hour plasma glucose ≥ 200 mg/dl during an OGTT

OR

- Random plasma glucose ≥ 200 mg/dl with classic symptoms of hyperglycemia (polyuria, polydipsia)

Table 1—*Criteria for the diagnosis of diabetes*

1. Symptoms of diabetes and a casual plasma glucose ≥200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

OR

2. Fasting plasma glucose ≥126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

OR

3. 2-h plasma glucose ≥200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test. The test should be performed as described by the World Health Organization, using a glucose load of 75 g anhydrous glucose dissolved in water or 1.75 g/kg body wt if weight is <40 pounds (18 kg).

HgbA1C	Average Sugar
4	60
5	90
6	120
7	150
8	180
9	210
10	240
11	270
12	300
13	330

DIAGNOSTIC CRITERIA FOR PREDIABETES

- Fasting Plasma Glucose between 100 mg/dl and 125 mg/dl
- 2 hour plasma glucose between 140 mg/dl-199 mg/dl in the oral glucose tolerance test
- A1C 5.7-6.4%

TYPE 1 VS TYPE 2 DIABETES

Type 1 Diabetes	Type 2 Diabetes
Occurs when the pancreas is not able to produce enough insulin	Occurs due to insulin resistance (i.e. when the body does not respond well to insulin
Tends to develop at a younger age (childhood/adolescence)	Tends to develop at an older age
Cannot be prevented (there is a medication available to delay onset)	Lifestyle changes can help prevent
Autoimmune condition – typically antibody positive	Not autoimmune
Ketoacidosis is common	Ketoacidosis is uncommon
Concordance in identical twins: 50%	Concordance in identical twins: 90%
Requires insulin therapy	Can be managed with lifestyle modifications, oral medications, GLP-1 agonists, SGLT2 inhibitors, insulin
Both share symptoms of frequent urination, increased thirst, unintentional weight loss, fatigue, blurry vision Both have risk of complications if left untreated	

CONTENTS

- Incidence and Prevalence
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- Diagnostic Criteria
- **Management**

DAILY DIABETES TASKS – TYPE 1 DIABETES

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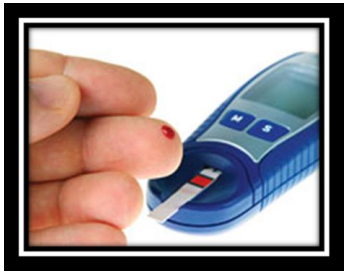
BLOOD SUGAR MONITORING

When to check:

- Before meals
- Before bedtime
- Before and after exercise
- During illness
- Having symptoms of hypoglycemia or hyperglycemia
- 2 am when fasting blood sugars have been elevated, change in insulin doses, extra physical activity, instructed by doctor or diabetes educator



TARGET BLOOD SUGAR LEVELS

Fasting (before meals)	Bedtime/Overnight)
90-130 mg/dl	90 – 150 mg/dl

INSULIN THERAPY

INSULIN AT SCHOOL

- Most children will receive a dose of insulin before lunch
- At least Novolog, Humalog, FIASP, Luymjev (rapid acting insulin to cover meals)
- Some children will receive their long acting insulin at lunch (Lantus, Basaglar, Semglee, Tresiba)

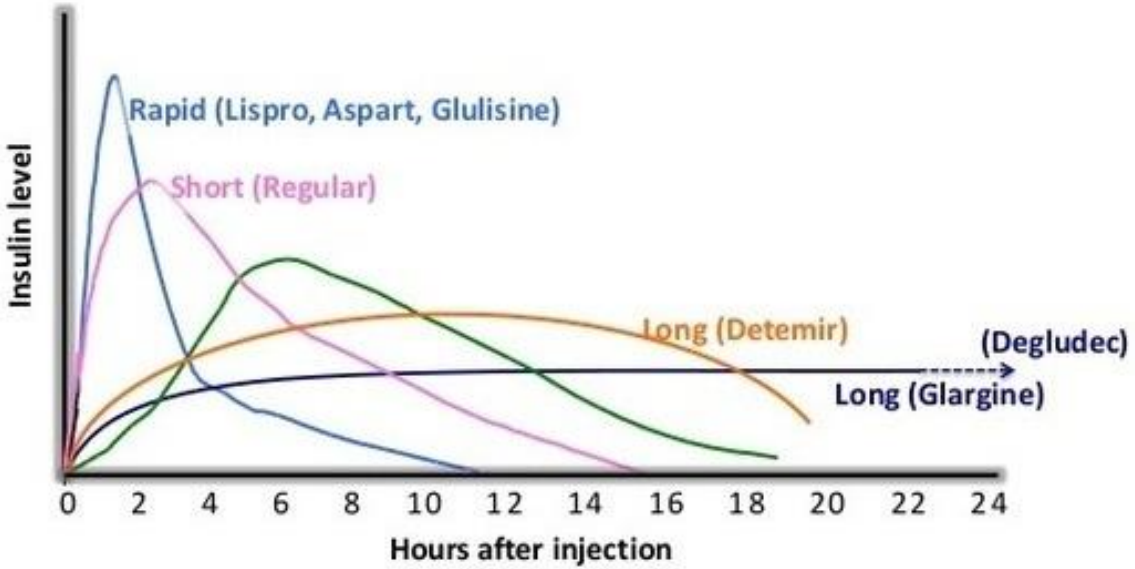
TYPES OF INSULIN

- **Long Acting**
  - Lantus
  - Basaglar
  - Semglee
  - Levemir
  - Tresiba

- **Rapid Acting**
  - Humalog
  - Novolog
  - Apidra

- **Ultra-Rapid Acting**
  - FIASP
  - Lyumjev

INSULIN THERAPY



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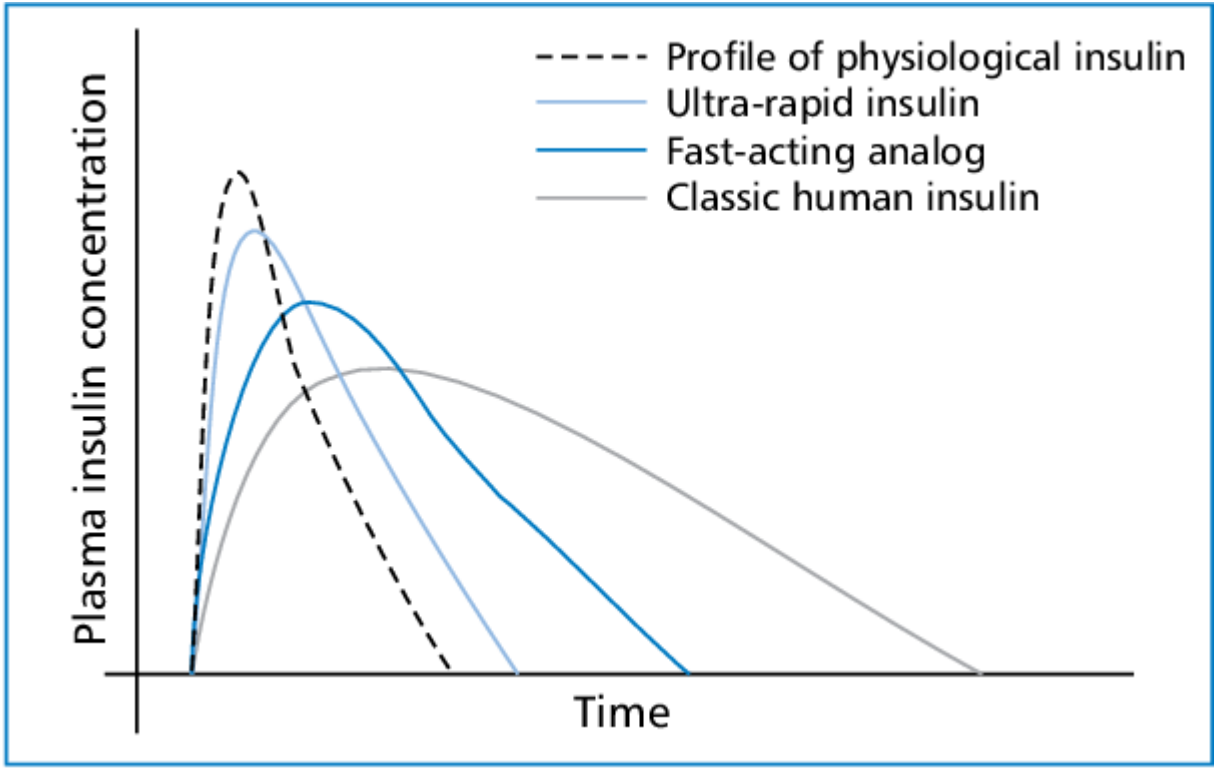
PROFILES OF ACTION OF DIFFERENT INSULIN TYPES



DAILY DIABETES TASKS – TYPE 2 DIABETES

- May require blood glucose monitoring if on insulin
- Treatment
  - Lifestyle modification – diet/exercise
  - Oral Medication – Metformin
  - Insulin may be required depending on blood glucose levels
  - GLP-1 agonists (ex: Victoza)
  - SGLT2 inhibitor (Empagliflozin)
- Metabolic Surgery

DIABETES COMPLICATIONS

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COMPLICATIONS OF POORLY CONTROLLED DIABETES

- Retinopathy
- Nephropathy
- Neuropathy
- Dyslipidemia
- Hypertension

ASSOCIATED CONDITIONS

ASSOCIATED CONDITIONS IN TYPE 1 DM

- Thyroid Disease
  - Most common autoimmune disorder associated with diabetes (17-30%)
- Celiac Disease
  - 1.6-16.4% frequency in patients with Type 1 diabetes
- Addison Disease
  - Rare, primary adrenal insufficiency

DIABETES TECHNOLOGY

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DIABETES TECHNOLOGY- INSULIN PUMPS

Insulin pump

- Infusion sets and reservoirs - change every 1-3 days
- Basal rate – small amount of background insulin delivered continuously
  - Temp rate – adjust basal rate for a pre-determined period of time
    - (exercise, illness, stress, menstrual cycle)
- Bolus – dose of insulin delivered when needed (meal and/or correction)
  - Extended – feature used for certain meals such as high-fat

DIABETES TECHNOLOGY – CONTINUOUS GLUCOSE MONITORS

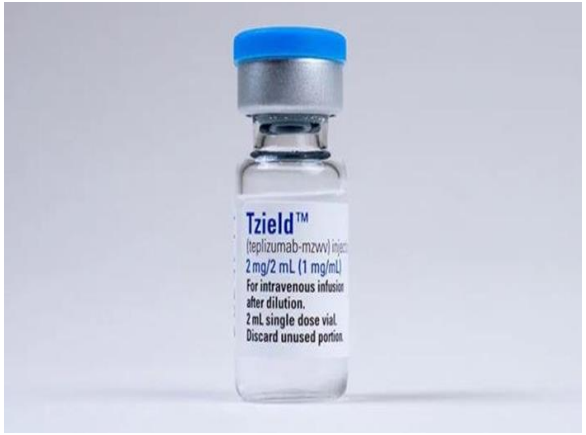
- Sensor – changed every 10-14 days
- Transmitter
- Receiver – specific insulin pumps, smart phone, smart watch, Dexcom receiver

SYSTEM	SYSTEM COMPONENTS	SENSOR	APPLICATOR	GLUCOSE READINGS
FreeStyle Libre 3	Sensor + App*	Size: 21 x 2.9mm	One piece applicator	Real-time glucose reading sent every minute to smartphone*
FreeStyle Libre 2	Sensor + Reader	Size: 30 x 5 mm	Two piece applicator	Scan to see glucose readings

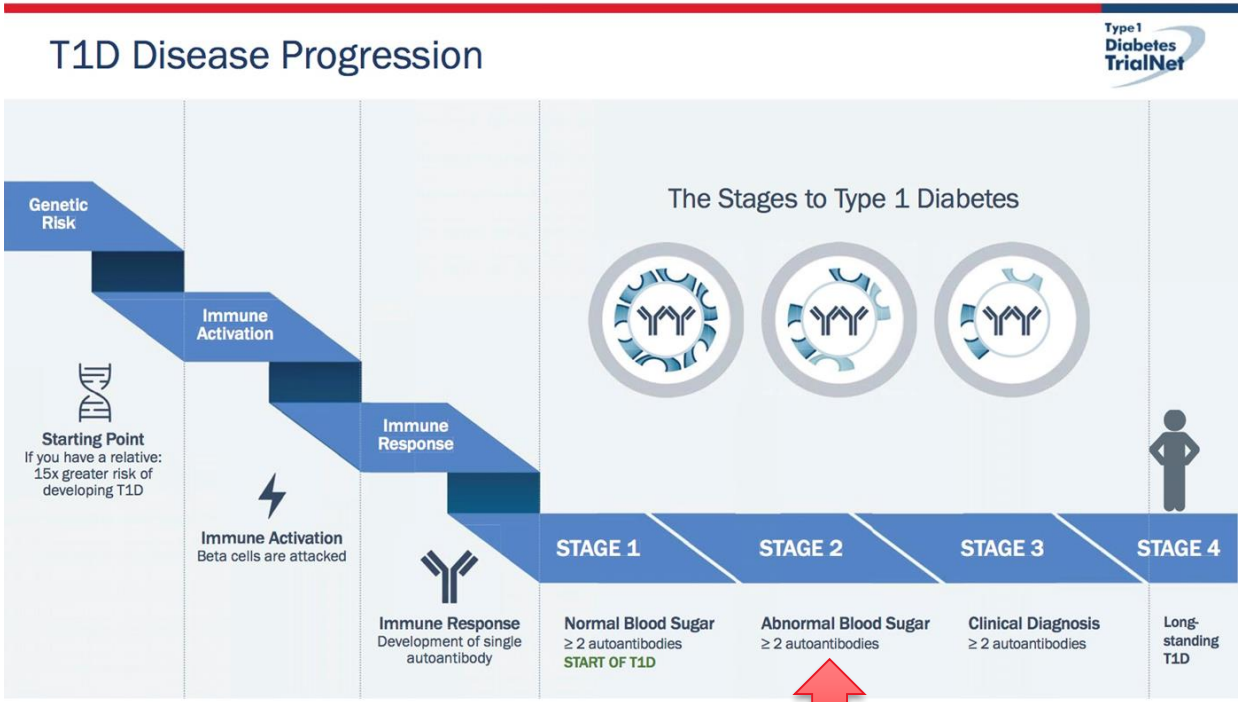
TYPE 1 DIABETES PREVENTION – TZIELD ™

- For the first time, there is a disease-modifying therapy for T1D.

- Teplizumab, manufactured under the brand name Tzield, is approved for use in delaying Stage 3 T1D in at-risk individuals
  - 2+ Insulin AAbs
  - Dysglycemia



TIMING FOR USE OF TZIELD™



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COMMENTS/QUESTIONS?