

Management of Type 1 Diabetes

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Objectives

- Discuss the prevalence of T1DM in the US
- Diagnose T1DM
- Differentiate between T1DM and other types
- Choose appropriate glycemic targets
- Calculate insulin doses for T1DM
- Discuss insulin delivery devices
- Discuss continuous glucose monitors
- Manage hypoglycemia
- Discuss the use of ketone testing in T1DM

United States T1DM Statistics

- 1.25 million Americans
- By 2050: 5 million
- 40,000 new cases each year
- 200,000 under age 20 have T1DM
- By 2050: 600,000
- 21% increase from 2001-2009

Genetic Risk Factors in T1DM

- Chromosome 6p21
- Concordance for monozygotic twins is 50% and 8% dizygotic
- Variants of Human leukocyte antigen complex
 - genes provide instructions to make proteins that play role in immune system
- Haplotypes that increase risk T1DM: (combination of HLA genes)
 - HLA-DQA1, HLA-DQB1, HLA-DRB1 combination is highest risk for T1DM
 - HLA-DR3 or HLA-DR4 puts Caucasians at high risk
 - HLA-DR 7 put African Americans at risk
 - HLA-DR 9 increase Japanese at high risk
- Mother w T1DM: child risk 1 in 25
- Father w T1DM: child risk 1 in 17
- Child's risk doubled if parent dx before age 11
- Both partners w T1DM: child risk is 1 in 4-10
- Family members w T1DM have 15 x higher risk than general population
- 1 in 7 w T1DM have type 2 polyglandular autoimmune syndrome
 - Thyroid disease, adrenal insufficiency, other immune disorders

Environmental Triggers

- Viral infection: coxsackie B4, congenital rubella, mumps
- Environmental toxins
- Cow's milk formulas

Clinical Presentation

- Broad range of signs and symptoms from very mild to coma
- Polyuria
- Polydipsia
- Polyphagia
- Weight loss
- Fatigue
- Irritability
- Diabetic ketoacidosis



Diagnosis of Diabetes

	Normal	Pre Diabetes	Diabetes
Fasting	< 100	100-125	126+
Postprandial	< 140	140-199	200+
HbA1c	<5.7	5.7-6.4	6.5%+

- If classic symptoms of hyperglycemia or hyperglycemic crisis or random plasma glucose 200+ mg/dL
- In absence of unequivocal hyperglycemia, diagnosis requires 2 abnormal test results from same sample or in 2 separate test samples

Estimated Average Glucose Values

AG mg/dL = $28.7 \times A1c - 46.7$

Causes of Inaccurate HbA1c

- Hemoglobin variants
- Sickle cell disease
- Pregnancy 2nd or 3rd trim
- Postpartum
- Glucose-6 phosphate dehydrogenase deficiency
- HIV
- Hemodialysis
- Recent blood loss
- Blood transfusion
- Erythropoietin therapy

Other Tests:

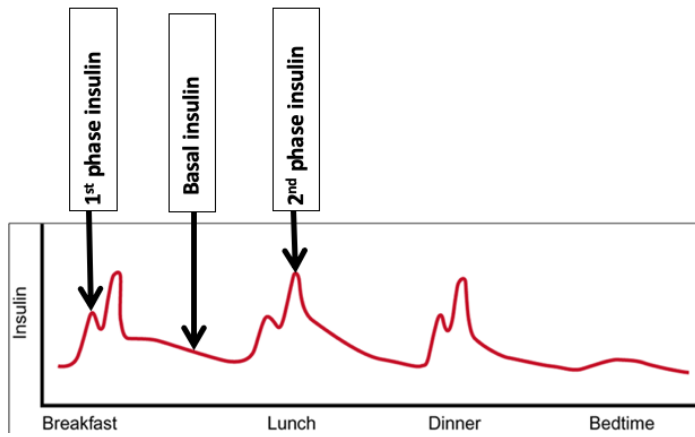
- C-peptide (measures insulin production by pancreas)
- Urine or blood ketones
- Antibodies
 - Islet Cell Antibodies (ICA): against cytoplasmic proteins in beta cells
 - Glutamic Acid decarboxylase (GAD-65)
 - Insulin autoantibodies IAA
 - Insulin autoantibody IA-2A:
 - Zinc transporter isoform ZnT8
 - 2 or more autoantibodies predicts clinical diabetes

Assess for Other Autoimmune Conditions if suspected

- Thyroid: check soon after dx then every 1-2 years
 - antithyroid peroxidase, antithyroglobulin antibodies, and TSH
- Celiac: check soon after dx then every repeat within 2 years then again after 5 years, more often if sx or family hx
 - IgA tissue transglutaminase (tTG) antibodies with normal total serum IgA levels
 - IgG to tTG and deamidated gliadin antibodies if IgA deficient
- Other autoimmune conditions: check if suspected
 - Addison
 - Autoimmune hepatitis
 - Autoimmune gastritis
 - Dermatomyositis
 - Myasthenia gravis

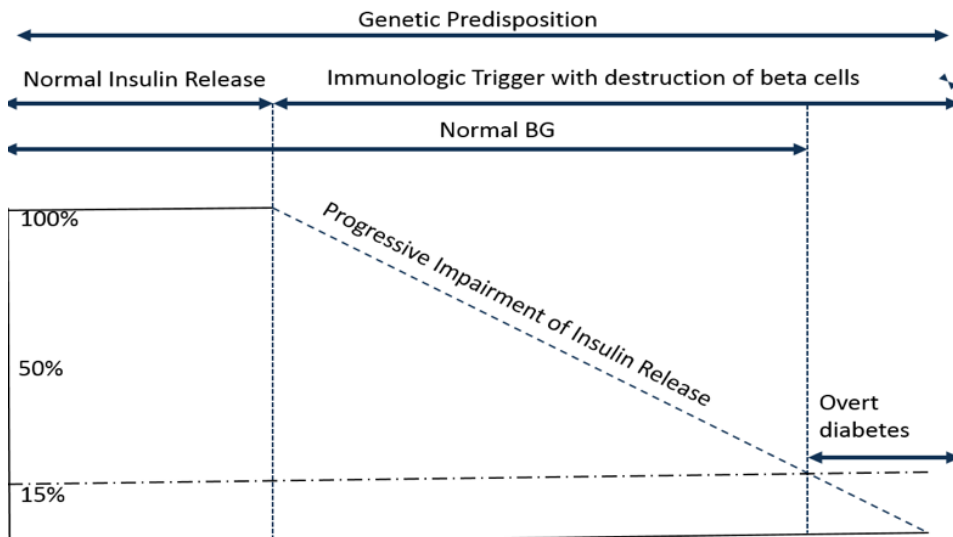
Normal Insulin Secretion

- Insulin is a peptide hormone produced by the β cells of the pancreatic islets of Langerhans
- Basal insulin secretion maintains normoglycemia between meals
- Bolus insulin secretion: to maintain normoglycemia after eating
 - First Phase insulin secretion:
 - premade insulin stored in secretory granules is released in the first 15 minutes following BG elevation
 - Second phase insulin secretion:
 - New insulin is manufactured and released over a more prolonged period of time
- In non-DM: peak postprandial blood insulin level occurs $\frac{1}{2}$ to $1\frac{1}{2}$ hours returning to basal levels at about 3 hours.



Stages of T1DM

	Stage 1	Stage 2	Stage 3
Characteristics	Autoimmunity <u>Normoglycemia</u> <u>Presymptomatic</u>	Autoimmunity <u>Normoglycemia</u> <u>Presymptomatic</u>	Hyperglycemia Symptomatic
Diagnostic Criteria	Multiple autoantibodies No IGT or IFG	Multiple autoantibodies <u>Dysglycemia IFG</u> and/or IGT	Clinical symptoms Diabetes by standard criteria



Preventing T1DM: TrialNet

- Pathway to Prevention study
- Abatacept
- Hydroxychloroquine
- Teplizumab

Glycemic Targets for T1DM

- Before meals: 90-130 mg/dL
- Bedtime/overnight: 90-150 mg/dL
- HbA1c target need to be individualized based on risk/history of hypoglycemia
- Check postprandial glucose if discrepancy between HbA1c and premeal blood glucose

Initiating Insulin Therapy

Units/Kg/D	Patient
0.5	Conditioned athlete, honeymoon phase
0.6	Motivated exerciser, woman in 1 st phase follicular cycle
0.7	Women in luteal phase or 1 st trimester <u>preg</u> , adult mildly ill with virus, child starting puberty
0.8	Women in 2 nd trimester <u>preg</u> , adult with severe infection
0.9	Women in 3 rd trimester <u>preg</u> , adult with bacterial infection
1.0	Women at term <u>preg</u> , adult with severe bacterial infection or illness, child at peak puberty
1.5-2.0	Child at peak puberty who is ill

1. Calculate total daily dose: 0.4-1 unit per kg
2. Divide the total daily dose into basal and bolus
3. Calculate an insulin to carbohydrate ratio
 - a. $450 \div \text{total daily dose} = \text{ICR}$
4. Calculate a correction/sensitivity factor
 - a. $1700 \div \text{total daily dose} = \text{initial correction factor}$
5. Choose a target blood glucose

Example: New dx T1DM: weight 80 kg

- $80 \text{ kg} \times 0.5 \text{ units} = \text{total dose/day } 40 \text{ units}$
- Basal dose: (50% of total dose) 20 units
- Insulin to carb ratio: $450 \div 40 \text{ units} = 11$
- Sensitivity factor: $1700 \div 40 = 42$
- Choose target blood glucose

Putting it together

- BG 187 mg/dL
- Carbs: 60
- Target BG: 100 mg/dL
- Food: $60 \div 11 = 5.45$
- BG correction: $187 - 100 \div 42 = 2$
- Add together: 7.45 round up or down depending on activity

Honeymoon

- At diagnosis, exogenous insulin requirements are large
- After hyperglycemia, ketosis/acidosis is corrected, remaining beta cells recover and produce insulin
- Duration of honeymoon is variable: early diagnosis and good BG control helps to prolong honeymoon

INSULIN

RAPID ACTING

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
Aspart	Fiasp	Yes 1000 units/10mL	Fiasp Flextouch 1u increment Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days
Aspart	Novolog	Yes 1000 units/10mL	Novolog FlexPen 1 u increment Max 60 3mL/300 units/pen 5 pens/box = 1500	Penfill for NovoPen Echo 0.5 u increments max 30 3mL/300 units/pen 5 pens/box = 1500	28 days
Glulisine	Apidra	Yes 1000 units/10mL	Apidra Solostar 1 u increment Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days
Lispro	Admelog	Yes 1000 units/10mL	Admelog Solostar 1 u increment Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days
Lispro	Humalog	Yes 1000 units/10mL	Humalog KwikPen 1 u increment Max 60 3mL/300 units/pen 5 pens/box = 1500	Cartridge for Autopen Classic Model AN3810 1 u increment max 21 Classic Model AN 3800 2 u increment max 42 HumaPen Luxura HD 0.5 u increment max 30 3mL/300 units/pen 5 pens/box = 1500	28 days
Lispro U-200	Humalog U-200	No	Humalog KwikPen U-200 1 u increment Max 60 3 mL/600 units/pen 2 pens/box = 1200	No	28 days

Inhaled Rapid Acting Human Insulin

Injected Mealtime insulin Dose	Afrezza Dose	# of 4 unit blue cartridges	# of 8 unit green cartridges
Up to 4 units	4 units	1	0
5-8 units	8 units	0	1
9-12 units	12 units	1	1
13-16 units	16 units	0	2
17-20 units	20 units	1	2
21-24 units	24 units	0	3

Afrezza sold in the following forms:

- 60 – 4 unit cartridges with 2 inhalers: NDC 47918-004-02
- 90 - 4 unit cartridges with 2 inhalers: NDC 47918-004-03
- 90 - 8 unit cartridges with 2 inhalers: NDC 47918-008-03
- 90 – with 60 as 4 unit cartridges and 30 as 8 unit cartridges: NDC 47918-048-12
- 90 – with 30 at 4 unit cartridges and 60 as 8 unit cartridges: NDC 47918-048-21
- 180 – with 90 as 4 unit cartridges and 90 as 8 unit cartridges: NDC 47918-048-33

SHORT ACTING

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
Regular U-100	Humulin R U-100 Novolin R Relion R	Yes 1000 units/10mL	No	No	31 days

CONCENTRATED REGULAR INSULIN

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
Regular U-500	Humulin R U-500	Yes 10,000 units/20 mL	Humulin R U-500 Kwikpen 5 u increment Max 300 3 mL pen = 1500 units/pen 2 pens/box = 3000 5 pens/box = 7500	No	40 days

INTERMEDIATE ACTING

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
NPH	Yes 1000 units/10mL	Yes 1000 units/10mL	Humulin N KwikPen 1 u increment max 60 3mL/300 units/pen 5 pens/box = 1500	No	Vial 31 days Pen 14 days
NPL	Found as part of premixed insulin				

LONG ACTING

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
Basiglar	Basiglar	No	Basiglar KwikPen 1 u increment Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days
Degludec	Tresiba U-100	No	Tresiba FlexTouch 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	8 weeks
Degludec U-200	Tresiba U-200	No	Tresiba FlexTouch U-200 2 u increments Max 160 3mL/600 units/pen 3 pens/box = 1800	No	8 weeks
Detemir	Levemir	Yes 1000 units/10mL	Levemir FlexTouch 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	42 days
Glargine	Lantus	Yes 1000 units/10mL	Lantus Solostar 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days
Glargine U-300	Toujeo	No	Toujeo Solostar 1 u increments Max 80 1.5 mL/450 units/pen 3 pens/box = 1500	No	28 days

COMBINATION

Generic Name	Brand Name	Vial	Pen	Penfill/cartridge	Dispose after
50% NPL, 50% Lispro	Humalog Mix 50/50	Yes 1000 units/10mL	Humalog KwikPen 50/50 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	Vial 28 days Pen 10 days
75% NPL, 25% Lispro	Humalog Mix 75/25	Yes 1000 units/10mL	Humalog KwikPen 75/25 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	Vial 28 days Pen 10 days
50% NPH, 50% Regular	Humulin 50/50	Yes 1000 units/10mL	No	No	31 days
70% NPH, 30% Regular	Humulin 70/30 Novolin 70/30 Relion 70/30	Yes 1000 units/10mL	Humulin 70/30 Kwikpen 1 u increments Max 60 3mL/300 units/pen 5 pens/box = 1500	No	Vial 31 days Pen 10 days
70% NPL, 30% Regular	Novolog Mix 70/30	Yes 1000 units/10mL	Novolog Mix 70/30 FlexTouch 1 u increments Max 60 3mL/300 units/pen 5 pens/box = 1500	No	Vial 28 days Pen 28 days
70% degludec; 30% aspart	Ryzodeg 70/30	No	Ryzodeg 70/30 FlexTouch 1 u increments Max 80 3mL/300 units/pen 5 pens/box = 1500	No	28 days

AMYLIN ANALOGUE

Generic Name	Brand Name	Dose Form Available	Starting	Maximum
Pramlintide	Symlin	0.1/mL injectable Sold in boxes of 2 pens with 2.7 mL per pen total 5.4 mL per box	T1DM start 15 mcg with meals \geq 30 gm CHO and titrate up by 15 mcg as tolerated T2DM 60 mcg with meals \geq 30 gms CHO	120 mcg with meals containing \geq 30 gms CHO

Adjusting Insulin Doses

- Is there a pattern?
- Is there any information you would want before making a change?
- Which column(s) is/are too high/low?
- Fix lows first
- What can be changed to fix the pattern of high/low?
- Change in 10-20% increments

Breakfast	Lunch	Supper	Bedtime
95	241	114	110
109	263	109	128
117	192	127	142
98	209	94	115

Breakfast	Lunch	Supper	Bedtime
178	97	114	110
286	86	109	128
265	102	127	142
223	146	94	115

Breakfast	Lunch	Supper	Bedtime
95	132	114	298
43	263	109	128
117	57	127	362
66	209	394	115

Reasons for Variable BG

- Not mixing cloudy insulin well enough
- Not mixing 2 kinds of insulin correctly
- Meter technique error
- Incorrect dosing
- Incorrect timing
- Variation in site
- Incorrectly estimated carbohydrate
- Growth spurts
- Reasons for Variable BG
- Weight change
- Reduced food intake without weight loss
- Activity change
- Stress
- Illness
- Steroids/certain medications
- Variability of long acting insulin
- Menstrual cycle

BG < 70 mg/dl: DM vs. Non DM

No Diabetes	T1DM or low C-Peptide
<ul style="list-style-type: none"> • Insulin levels drop • Glucagon secreted • Epinephrine release • Norepinephrine • Cortisol release • Growth hormone • Neurotransmitters 	<ul style="list-style-type: none"> • Insulin levels high • Glucagon not secreted • Epinephrine release • Norepinephrine • Cortisol release • Growth hormone • Neurotransmitter Hypoglycemia

- 20% of T1DM will die from hypoglycemia
- 40% of T1DM will have severe hypo if duration of > 15 years
- Annual rate of severe hypoglycemia requiring emergency medical services: 7.1%
- Mortality rate 1 year after severe hypoglycemia T1 & T2 combined = 17%

Hypoglycemia Symptoms

- Shaky
- Sweating
- Weakness
- Irritable/confusion
- Lethargy/unconsciousness

Tx of Mild Hypo: 15 grams simple CHO

- 4 glucose tablets
- 4 pieces hard candy
- 4 starburst
- 15 skittles
- ½ cup sweet drink/juice
- 1 tbsp honey, syrup, sugar

Severe Hypoglycemia Treatment

- Cause glycogen to be converted into glucose
- 1 kit raises BG ~ 50 mg/dl
- 1 Kit has 1 mg
- Given SC, IM, or IV
- 1 mg for child > 4
- ½ mg for child < 4
- Sites same as insulin
- Push needle in all way

Mini Dose Glucagon

- Pt unable to swallow CHO but is awake & alert with BG < 80 mg
- 2 “units” for 1 yo
- 1 “unit” per year of age for 2 years & older
- Max 15 “units”
- If not above 80 mg/dL in 30 min, double the dose (max 30)

Nasal Glucagon

- Glucagon nasal powder (Baqsimi) 3 mg one time use
- Approved for age 4+
- Approved 7/24/2019

Beta-hydroxybutyrate: NovaMax

0.6 – 1.5 = call MD

> 1.5 = go to EC

