



Type 1 Diabetes

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Work Disclosures

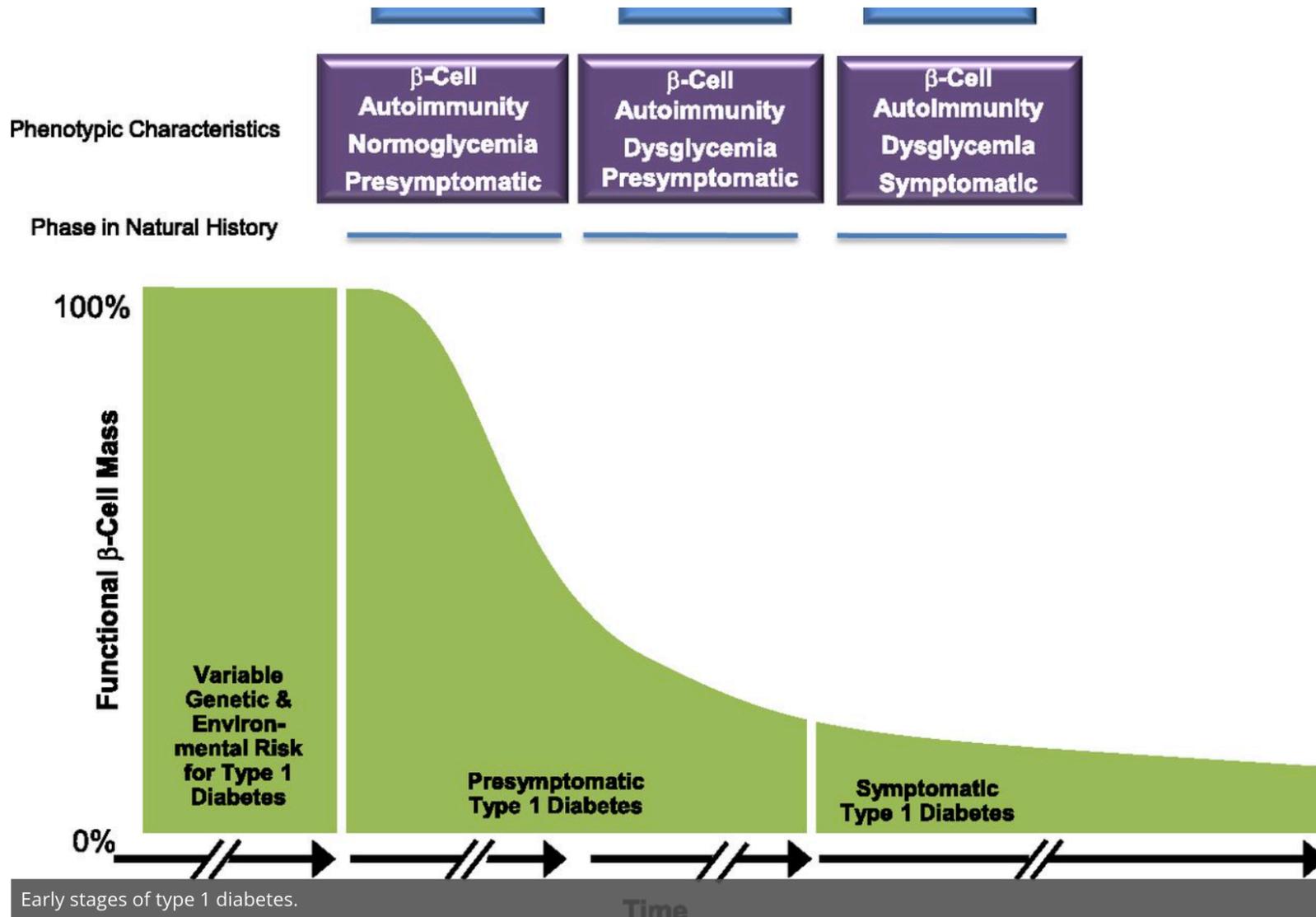
- I receive salary support from Novo Nordisk for an investigator-initiated study.
- I have received free supplies from Dexcom for previous investigator-initiated research.

Personal Disclosures

- I have type 1 diabetes.

- Basic pathophysiology of type 1 diabetes
- Differentiate between type 1 and type 2 diabetes
- Sick day management in type 1 diabetes
- Management of hypoglycemia in type 1 diabetes
- Association of type 1 diabetes and other autoimmune conditions
- Basic diabetes technology

Three Stages of Type 1 Diabetes



Lower Glucose

- ~~Insulin~~
- ~~Glucagon~~
- Incretins (indirectly)
 - ~~GLP-1~~
 - ~~GIP~~

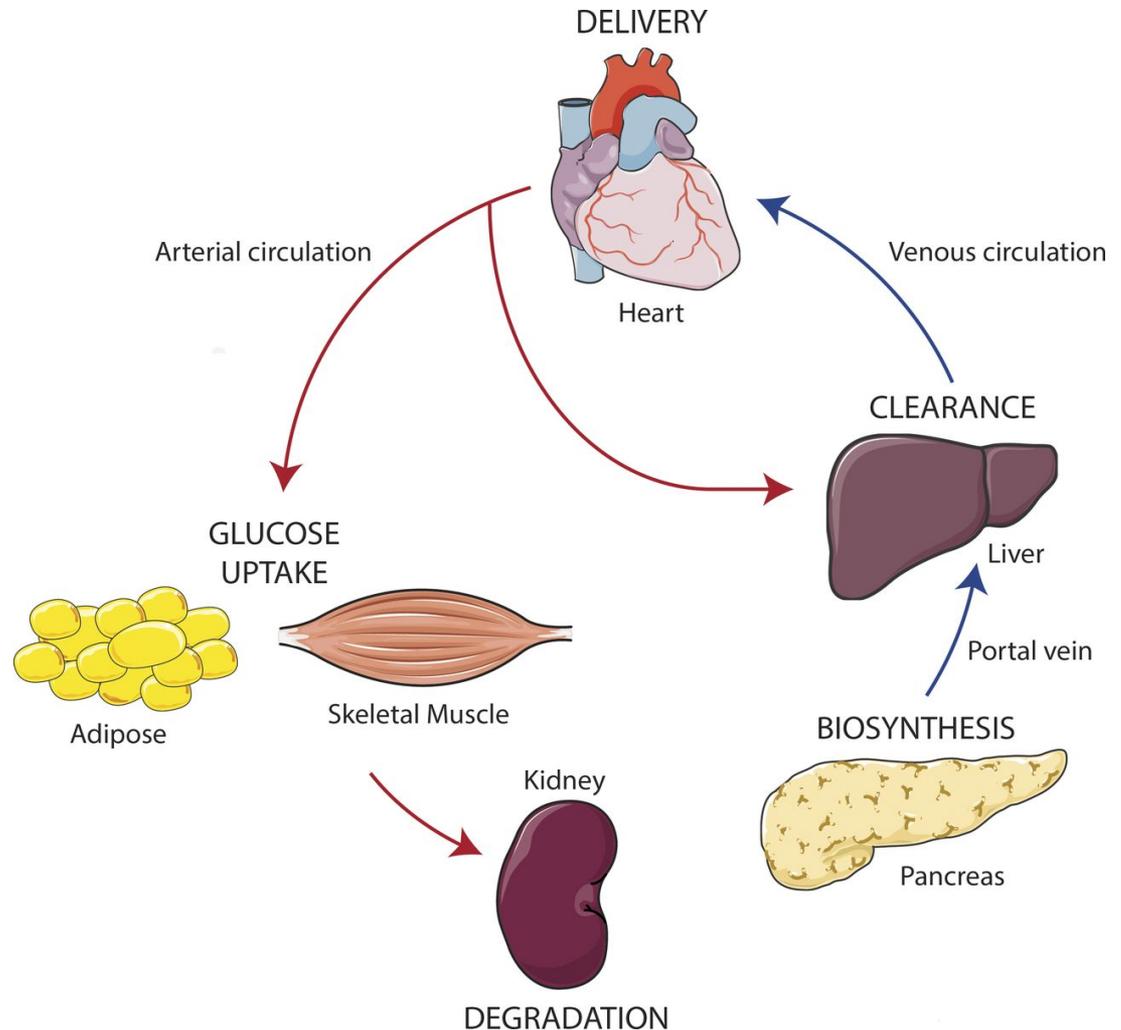
Raise Glucose

- ~~Glucagon~~
- Cortisol
- Epinephrine ?
- Norepinephrine ?
- Growth Hormone

**Individuals with T1D don't produce insulin & have abnormal glucagon secretion which make glycemic changes difficult to anticipate.
Epi & Norepi are sometimes dysregulated**

Insulin

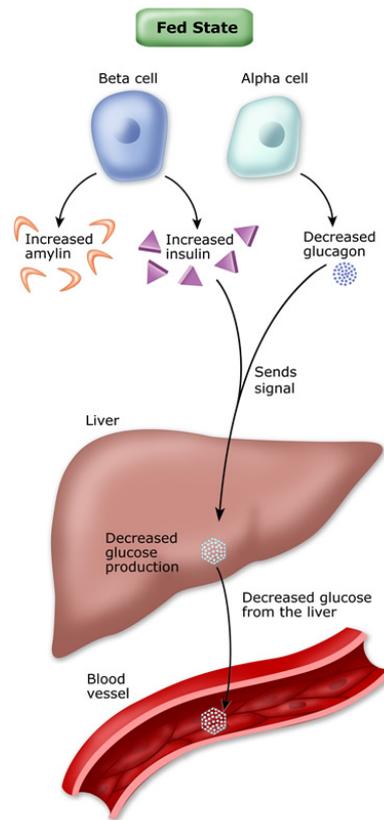
- Increase glycogen stores in muscle and liver
- Increase protein synthesis in muscle
- Increase lipid synthesis in adipose tissue (uptake of triglycerides)



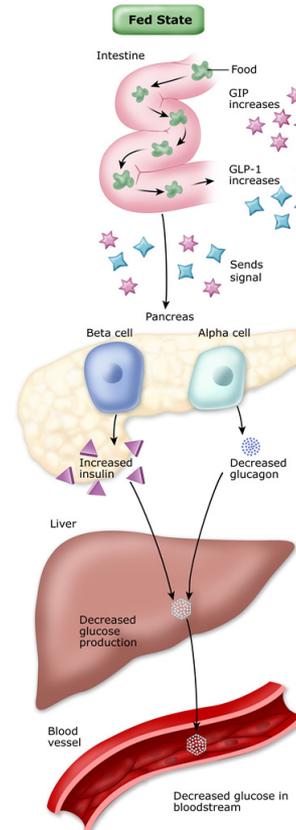
Amylin

- Secreted with insulin from pancreatic beta cells
- Reduces secretion of glucagon
- Slows gastric emptying (emptying of food from stomach to small intestine where carbohydrates are absorbed)

The Effect of Amylin



The Effect of GLP-1 and GIP



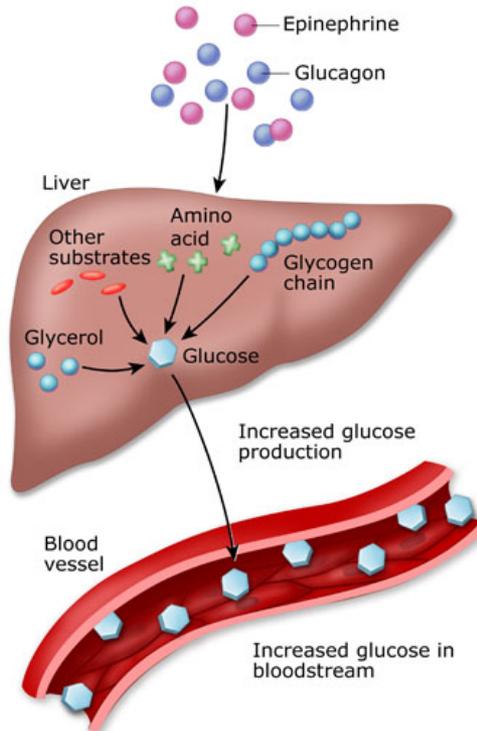
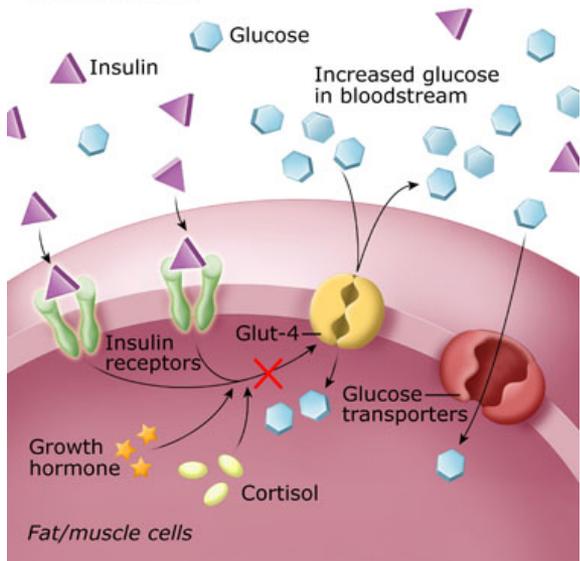
GLP-1 (glucagon-like peptide 1)

- Made in the stomach
- Slows gastric emptying
- Increases insulin secretion

GIP (gastric inhibitory peptide)

- "Incretin" hormone
- Stimulates insulin secretion when blood sugars are high
- Decrease gastric acid secretion
- Slows gastric emptying

Glucose Counter-regulatory Hormones: Effect on Fat and Muscle Cells



Hypoglycemia or **stress** can lead to rapid release of epinephrine* & glucagon*, followed by a more slow release of growth hormone and cortisol, making tissues less sensitive to insulin. The glycemic effects of these hormones can last up to 6-8 hours in some studies.

*release of these hormones may not be predictable

Glucagon can be **INAPPROPRIATELY** released after meals, causing more extreme postprandial hyperglycemia despite appropriate insulin dosing for meals.

Must have 2 repeated tests or 2 separate tests

A1c level $\geq 6.5\%$

Fasting Plasma Glucose ≥ 126 mg/dL

2-hour plasma glucose ≥ 200 mg/dL during an oral glucose tolerance test (75 g anhydrous glucose dissolved in water)

In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random glucose ≥ 200 mg/dL

Supports T1D

- Not obese (though could be)
- Lack of hypertension, dyslipidemia
- No acanthosis nigricans
- Ethnic background with low prevalence of T2D (European, Caucasian)
- Family history of autoimmunity
- Low c-peptide levels
- Low insulin levels
- Positive autoantibodies (85-90% of T1D cases)

Supports T2D

- Metabolic Syndrome (Obesity, Hypertension, Dyslipidemia)
- Acanthosis Nigricans
- Ethnic background with high prevalence of T2D
- Strong family history of T2D, obesity, metabolic syndrome
- Typically do not present with DKA
- Higher c-peptide levels
- Higher insulin levels

CASE 1

- 16 mo previously healthy boy presented to pediatrician with tachypnea
- Coxsackie infection 2 weeks prior
- Received albuterol in the doctor's office and was sent home, but no resolution
- Vomited at home, and was sent to the ER
- No diarrhea or weight loss
- Endorsed polyuria/polydipsia
- Maternal GMA with hypothyroidism, paternal GPA with Grave's, paternal great GMA with lupus, paternal great aunt with type I DM

Physical Exam:

Temp: 37.3 °C, Pulse: 120, **Resp: 40**, SpO2: 100 %.

POCT glucose 579 mg/dL

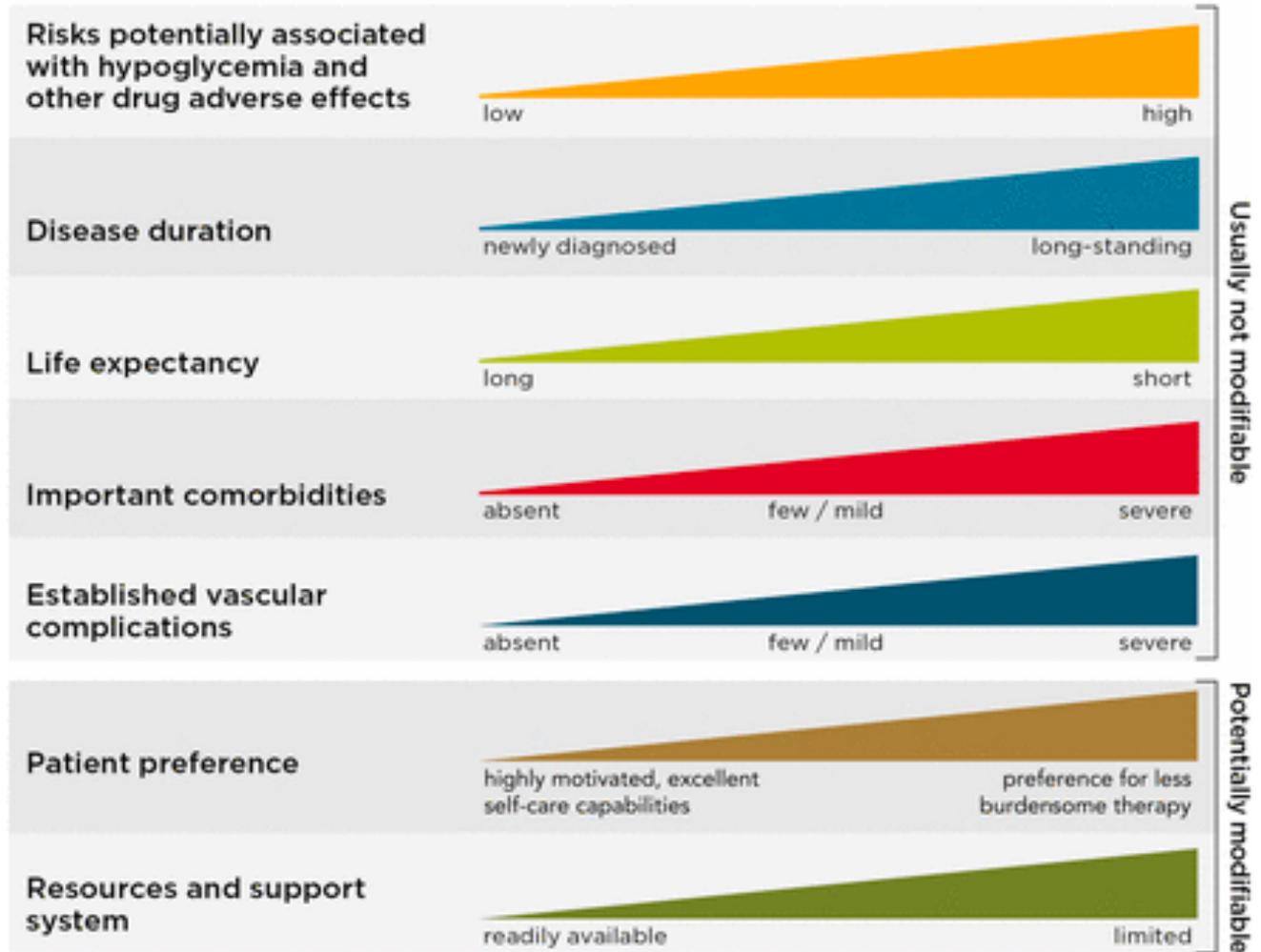
iSTAT pH 7.14, bicarb 6, Na 131, K 5.7

POC GENERAL		
pH, Venous (POC)		7.14 ▼
pCO2, Venous (POC)		17 ▼
pO2, Venous (POC)		56 ▲
HCO3 Calculated, V...		6.0 ▼
CO2 Calculated, Ve...		6.0 ▼
Base Excess, Venou...		-23
O2 Sat Calculated,...		80
POC Sodium	131	▼
POC Potassium	5.7	▲
POC Ionized Calcium	6.20	▲
POC Glucose	579	▲
POC Hematocrit	43.0	▲
Lactate, POC		3.3 ▲
CO2, POC	9.0	▼
POC BUN	22	▲
POC Creatinine	<0.2	▼
POC eGFR (Afr Amer)	Comment Only *	
POC eGFR (NON Afri...	Comment Only *	
Hemoglobin A1C, POC		

- When a family has a child that has just been diagnosed with diabetes, the family's life is forever changed
- Each family will respond to the diagnosis differently. Try to understand the family's perception & understanding of diabetes.
- It is important to let families know that any response they are having is normal. It is normal to feel a wide range of emotions.
- Parents & caregivers will have some degree of guilt. **Tell them it is not their fault.** Praise them for anything good that they did by bringing their child to medical attention.

Approach to Individualization of Glycemic Targets

Patient / Disease Features More stringent ← A1C 7% → Less stringent



Pediatrics
A1c Target $\leq 7.5\%$

Adults
A1c Target $\leq 7\%$

Both targets are WITHOUT severe hypoglycemia

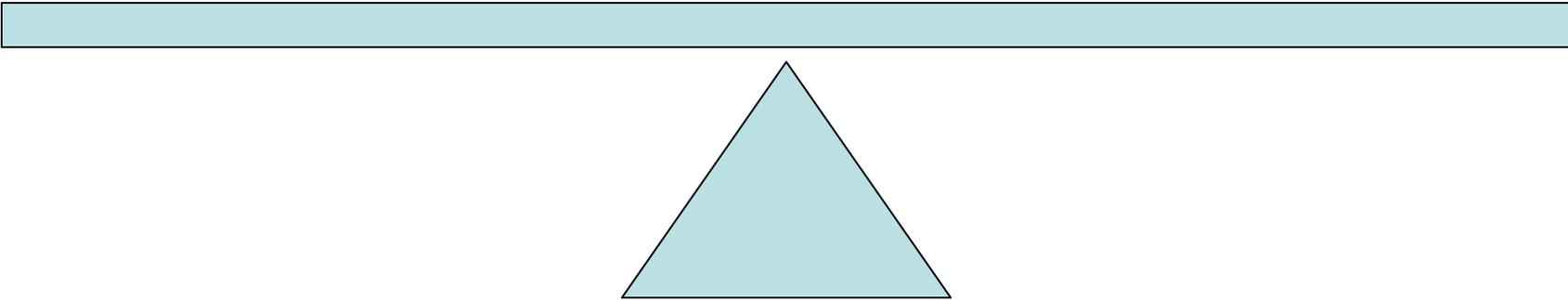
KETOSIS AND DKA

**For anyone with T1D,
vomiting is ketosis or DKA
until proven otherwise!!!**

**Ketones mean
YOU NEED MORE INSULIN!**

Insulin

Counter-regulatory
Hormones

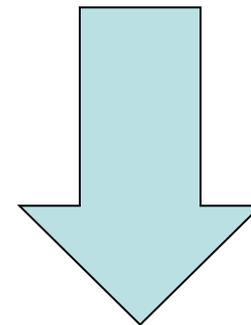
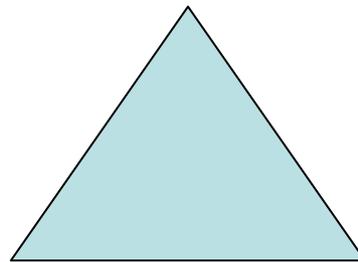
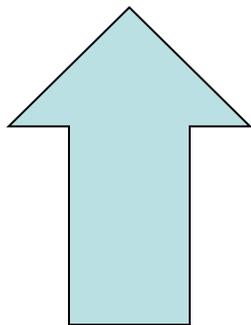


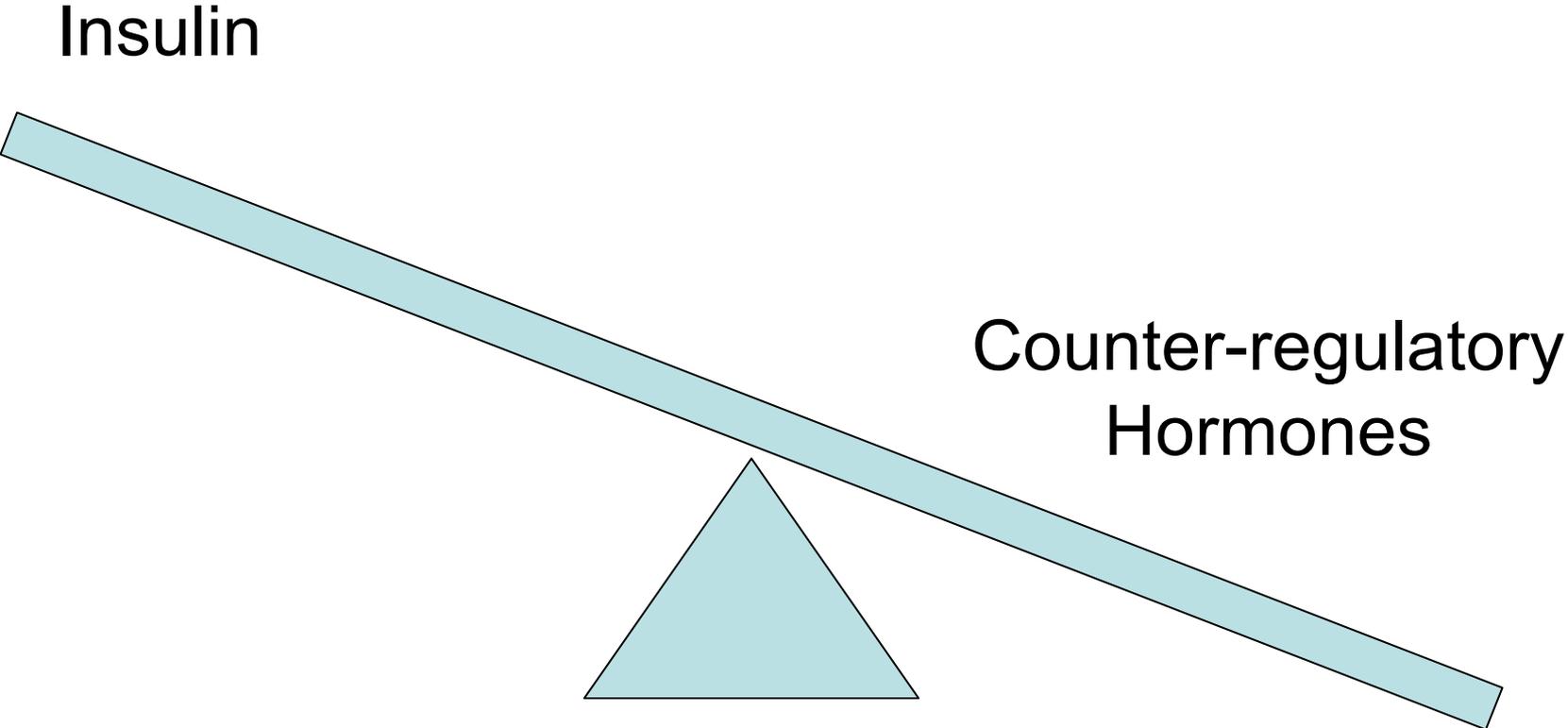
Insulin Deficiency

Missed doses
Lipohypertrophy
Insulin pump or
infusion site failure
Insulin exposed to
heat/cold or expired
(>30 days old)

Increased Counter- regulatory Hormones

Physiologic stress
Psychological stress
Infection/inflammation





- When to Call 911 or Go to the Emergency Room
 - Severe headache
 - Prolonged vomiting (more than 6 hours → getting dehydrated which will worsen acidosis)
 - Not urinating (sign of severe dehydration)
 - Trouble breathing (rapid, deep kussmaul's breathing)
 - Ketones not decreasing over time (large ketones more than 9 hours)
 - Not making sense or not waking up (altered mental status)

- Check ketones during ANY illness
 - Upset stomach, belly pain
 - Vomiting (even if isolated event)
- If glucose >250-300mg/dl for 2 consecutive blood tests
- BG > 250mg/dl prior to exercise
- Fruity breath, breathing quickly

**CALL ENDOCRINOLOGY
ANY TIME 24/7 IF KETONES
ARE MODERATE TO LARGE**

Pro tips:

1. Ensure ketone strips are not expired
2. Ensure ketone level read within 15 seconds (leaving ketone strips out can cause false elevations in ketone levels).



CASE 2

- Called by patient's family because patient ate pizza last night and started vomiting (non-bloody, non-bilious) overnight and this morning.
- Patient is a 16 yo F with type 1 diabetes, celiac disease

What additional history do you want?

Not Diabetes

Fever

URI symptoms

Diarrhea

Gluten

Obstructive symptoms

You Could Have Both!!!

Whenever a child with T1D is sick (with any illness), we recommend twice daily ketone checks to SCREEN for ketones.

DO NOT OMIT INSULIN UNLESS DISCUSSED WITH AN ENDOCRINOLOGIST

Diabetes

Hyperglycemia

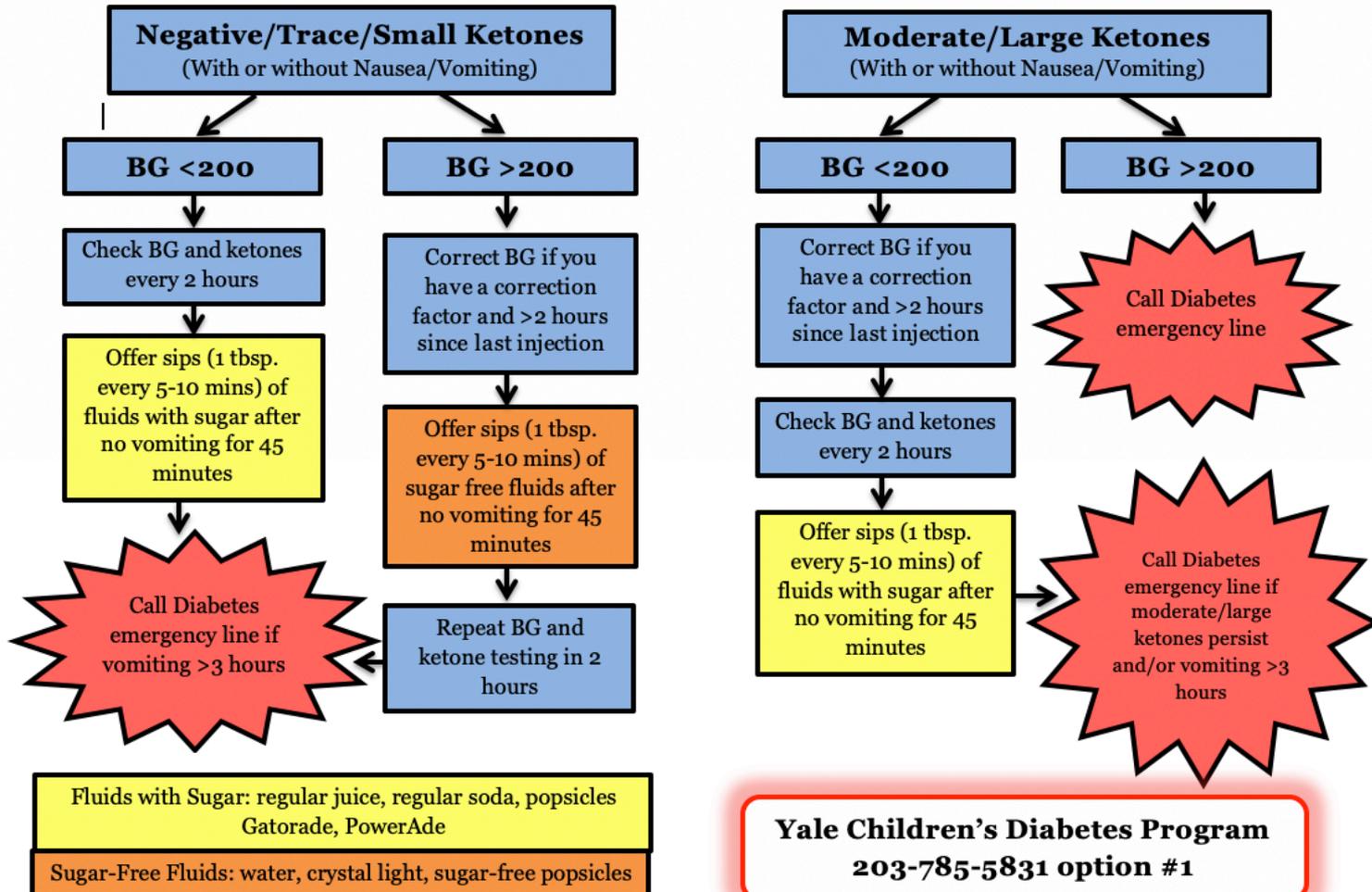
Moderate/large ketones

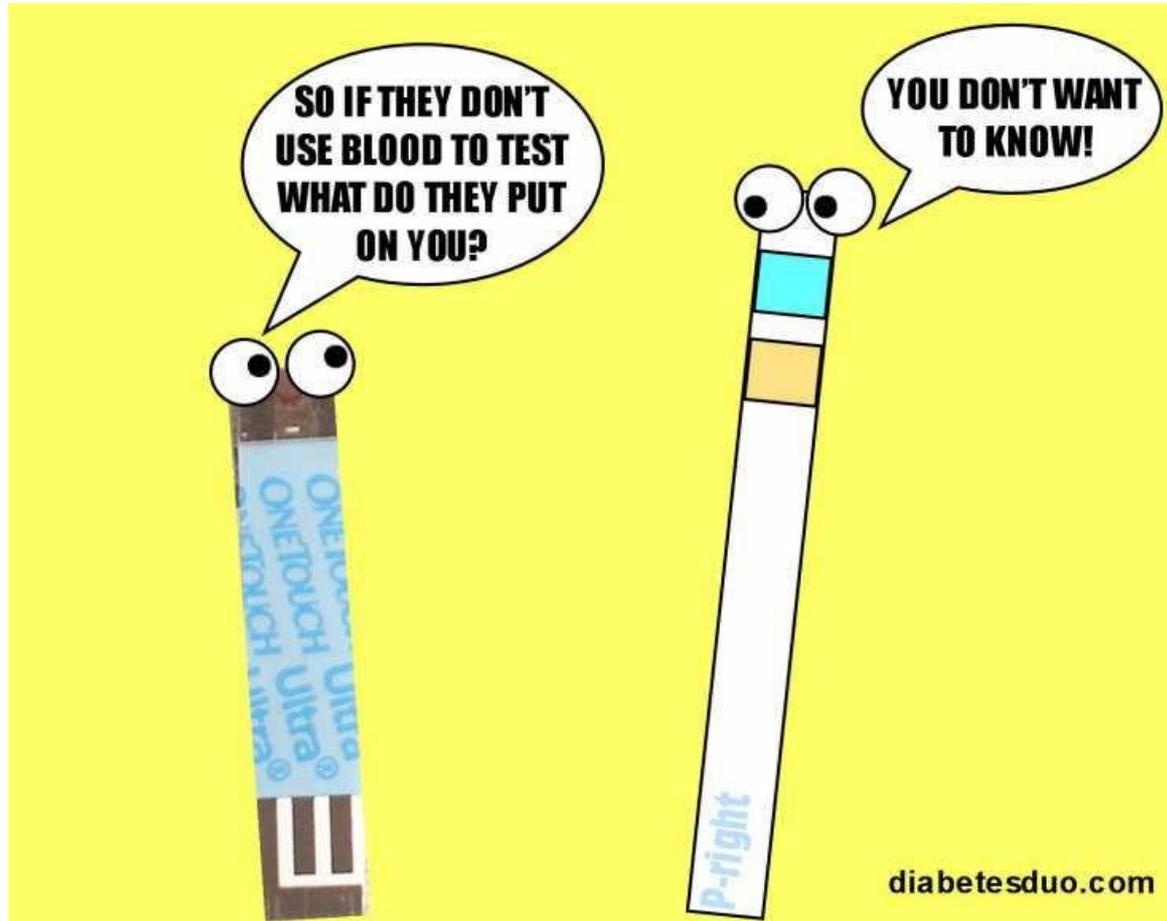


Sick Day on Injection Therapy

Blood sugar >300 first thing in am, 2 daytime BG's >300 2 hours apart, OR nausea/vomiting *always* Check Ketones!

**REMEMBER YOU STILL NEED SOME LONG ACTING INSULIN
(Lantus, Levemir, Tresiba, Basaglar or NPH)!**





- The background insulin your body makes to keep your blood sugars stable all day if you didn't eat anything.
- You need basal insulin EVERY DAY even if you are not eating
- **BASAL insulin is the most important insulin to prevent DKA**

Basal Insulin

Injection: Syringe/Pen

24 hours:

Degludec (Tresiba)

Glargine (Lantus)

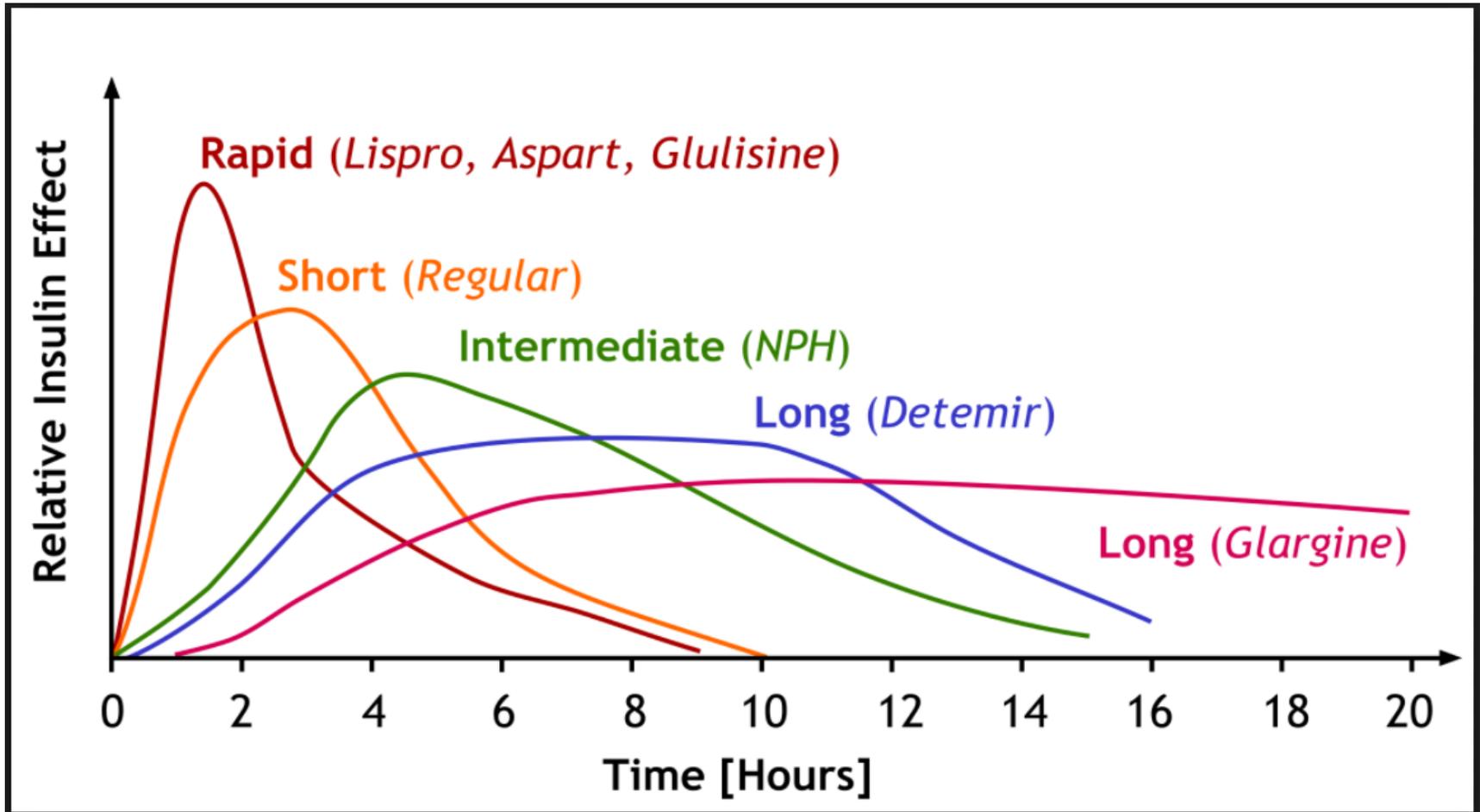
Basaglar

12 hours:

Detemir (Levemir)

Insulin Pump

Small amounts of rapid acting insulin are given every few minutes through an infusion pump to mimic a steady background insulin



Adapted from Hirsch IB. Insulin analogues. N Engl J Med. 2005;352(2):177.

- Total Daily Dose (TDD) – weight-based dosing (do not use ideal body weight)
 - 0.5 u/kg/day under 5 years
 - 0.5 - 1 u/kg/day pre-pubertal
 - 1 - 2 u/kg/day puberty
- 40-50% of TDD is “basal”
 - Lantus/Tresiba (glargine/basaglar/degludec)
 - Total 24-hour basal insulin for insulin pumps
- 50-60% is bolus insulin for carbohydrates & hyperglycemia treatment

- Insulin to carbohydrate ratio (IC Ratio) – 450 Rule
 - $450 / \text{TDD} = \text{carbohydrates covered by 1 unit of insulin}$
 - Can change throughout the day
- Insulin sensitivity factor (ISF) or hyperglycemia correction – 1800 Rule
 - $1800 / \text{TDD} = \text{the amount the blood sugar will be lowered by 1 unit of insulin}$
 - Target BG could be 100 mg/dL to 150 mg/dL depending on time of day, patient, etc.
 - Can change throughout the day

CASE 3

- A 12 year old girl weighing 50 kg presents with new onset type 1 diabetes.
- TDD = 50 kg x ~1 unit/kg/day = 50 units/day
- Basal: 40-50% of TDD, so 20-25 units/day is basal insulin
- Insulin to carbohydrate ratio
 - $450 / 20 = 9$
 - 1 unit will cover 9 grams of carbohydrates → round to 1u:10g
- Insulin sensitivity factor
 - $1800 / 50 = 36$
 - 1 unit of insulin will lower the blood sugar 36 mg/dL → round to 1u:35mg/dL

- 2 injections per day
- Avoid lunchtime dose (school may not have a nurse)
- Most simple regimen for family
- AM: Humalog or Novolog w/NPH
 - Covers Breakfast & Lunch
- PM: Humalog or Novolog w/Levemir
 - Covers Dinner & Basal needs
- Advantages
 - Relatively easy
 - Fewer injections (no lunch injection unless hyperglycemic)
- Disadvantages
 - Less flexibility with timing & amount of food for meals
 - NPH requires morning snack to prevent hypoglycemia
 - Less physiologic

- For many families, using a fixed amount of insulin for meals and a sliding scale will be easier
- Discuss the amount of carbohydrates that the patient typically eats for meals
- Calculate a the insulin for those meals and come up with a range
 - Small meal = 5 units
 - Medium sized meal = 10 units
 - Large meal = 15 units
- Sliding Scale for hyperglycemia
 - 150-200 – give 2 units
 - 201-250 – give 4 units
 - 251-300 – give 6 units
 - Etc...

Rule of 15's:

15g rapid acting carbs, recheck BG 15 minutes later

Repeat until BG > 70

ALWAYS keep a low treatment with you at ALL times just in case.



- GLUCAGON for emergencies – intranasal, IM or SQ injection if patient is seizing or unable to take PO when hypoglycemic
 - Glucagon may cause **vomiting** after giving a dose (esp 1mg dose)
 - Children under 6 yrs old or under 20 kg receive 0.5mg dose (half dose)
 - Recheck BG in 15 minutes, can repeat up to 3 doses if no response
 - **Glucagon needs to be followed by carbohydrate intake (restore liver glycogen) to prevent recurrence of hypoglycemia**

1 mg IM glucagon has an approximate **onset of action** of 8 to 10 minutes and a **duration** of 12 to 27 minutes.



3 Different Glucagon Rescue Options

Glucagon Emergency Kit | Powder + diluent



Glucagon Emergency Kit by **Lilly**



GlucaGen Hypo Kit by **NovoNordisk**

Gvoke Pre-Filled Pen or HypoPen Auto-Injector

Gvoke™ Pre-Filled Syringe
(glucagon injection)



Gvoke HypoPen™
(glucagon injection)



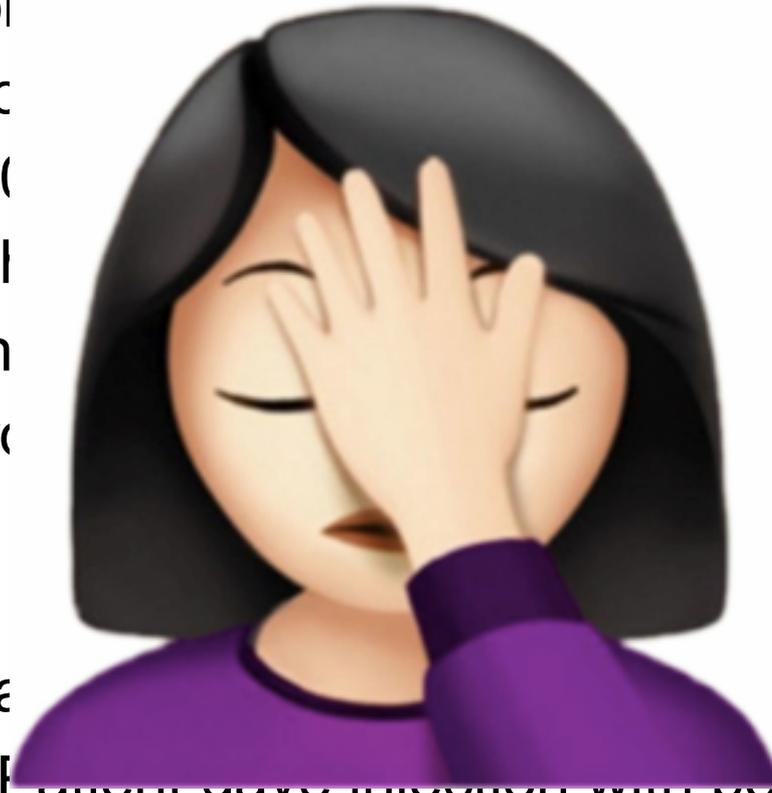
Baqsimi – Nasal Glucagon



Keep tube sealed until ready to use.

CASE 4

- 12 yo M with T1D
- Grandmother is primary caregiver
- Lots of psychosocial issues
- Patient’s A1c is 10%
- Patient says that he doesn’t want to take insulin
- Grandma finds snoring at night
- Signs point toward depression



Asked patient

are giving injections

Patient gave injection with pen in front of provider

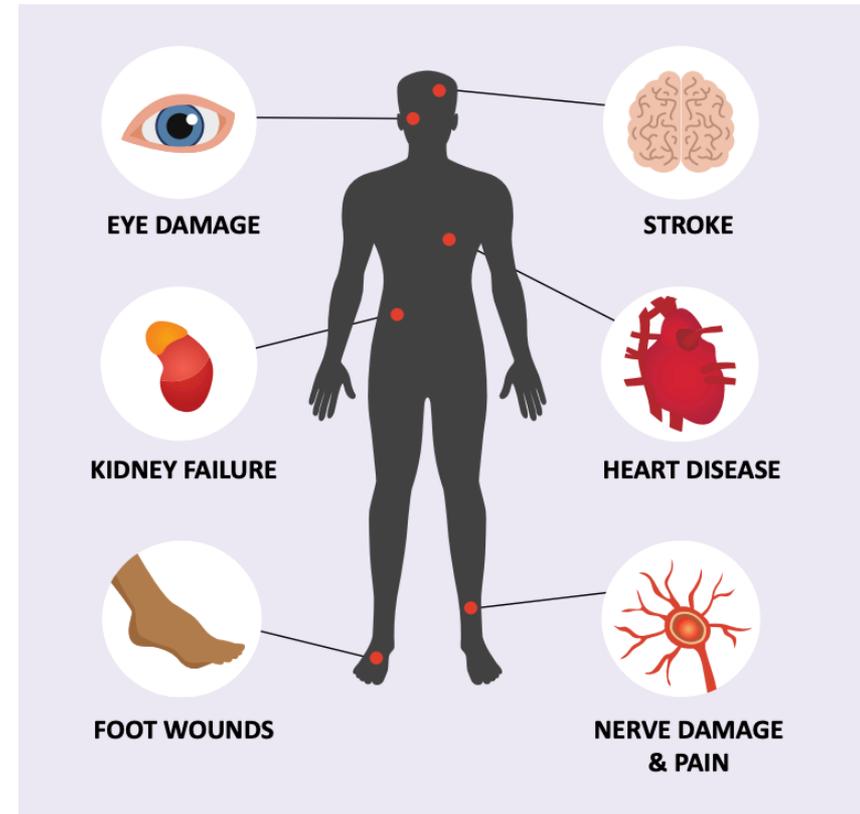
Did not hold pen in place after injecting

Insulin leaked everywhere

Provider asked if this happens every time? Patient stated yes!

- **Do not associate emotions or judgement with blood sugar values.** There are no “good” or “bad” blood sugars. The blood sugar number helps the patient figure out what to do – give insulin, have a snack, etc.
 - Instead of asking “what did you eat” or “what did you do wrong,” praise the child for checking their blood sugars.
- **Use simple organizational techniques to stay on top of diabetes.** Set phone reminders. Keep a checklist of diabetes supplies to take with you. Use a planner.
- **Balance blood sugar and mental health goals.** Type 1 diabetes is a 24/7 condition that is associated with high levels of burnout.
 - *“Managing diabetes is a marathon, not a sprint. I realized I had to trade off tighter control in the near term for a happier family and a child who doesn’t feel that her diabetes rules her life.” --Parent of a child with type 1 diabetes*

- **Listen to the teen and try to figure out what works for THEM.**
 - *“My challenge as a parent has been learning to listen to what works for her, and helping her make that a reality.” – Parent of a child with T1D*
- **Belaboring the risk of complications is NOT helpful**
 - Patients and their families should be aware of complications, but this should NOT be the focus of conversation when a child or teen is struggling



- **Autoimmune hypo/hyperthyroidism**

- 17-30% of individuals with T1D have autoimmune thyroid disease (2-5% of general population, women > men)
- Check TSH, FT4 after diagnosis (once glycemic control has been established)
- Some advocate for thyroid antibody screening as well
- Screen every 1-2 years or sooner if thyroid antibodies are positive or symptoms develop

- **Celiac disease**

- 1.6-16.4% of T1D population (0.3-1% of general population)
- Screening justified based on increased risk of osteoporosis, iron deficiency, growth failure, and *potential* increased risk of retinopathy and albuminuria
- Screen after initial diagnosis (false positives at diagnosis)
- Repeat screening at 2 years and 5 years after diagnosis
- Consider more frequent screening in children who have symptoms (unexplained hypoglycemia) or a first-degree relative with celiac disease
- Serum IgA, IgA TTG
- If IgA deficient, check IgG to TTG and deamidated gliadin

Monitor for these as clinically indicated:

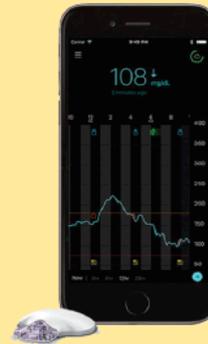
- Primary adrenal insufficiency
- Autoimmune hepatitis
- Autoimmune gastritis
- Dermatomyositis
- Myasthenia gravis



Dexcom G6



Eversense Implantable CGM

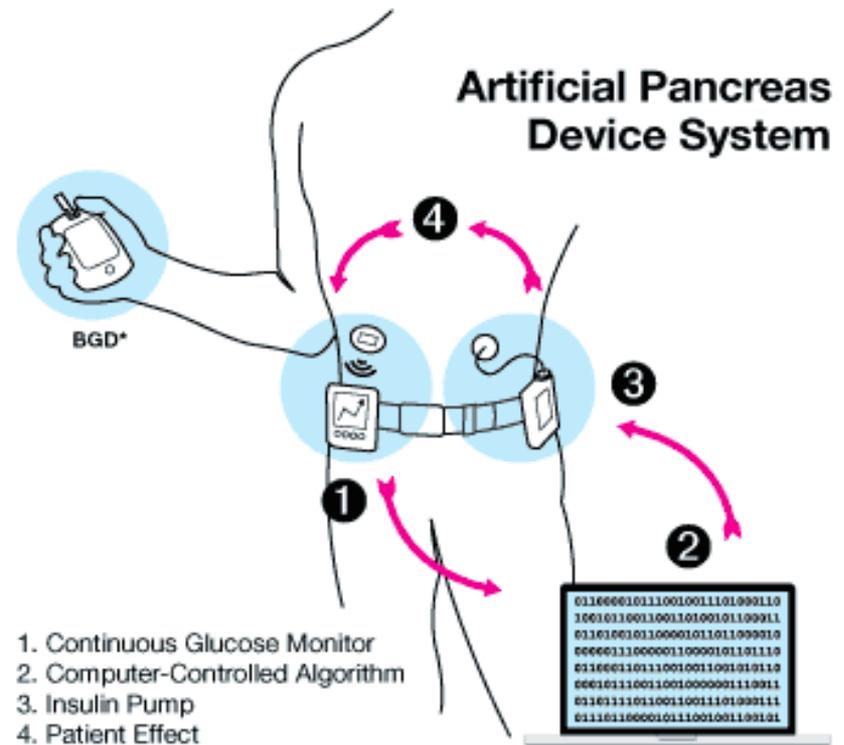


Medtronic Guardian



Abbott's FreeStyle® Libre

- Algorithm uses pharmacokinetic model of subcutaneous absorption & clearance of rapid acting insulin
- Future glucose levels are predicted and insulin infusion plan is mapped out
- After the first insulin delivery is given, glucose data is received (feedback) and modifications in the plan are made



Diabetes Care[®]

WWW.DIABETES.ORG/DIABETESCARE

JANUARY 2020

SUPPLEMENT

1

AMERICAN DIABETES ASSOCIATION

STANDARDS OF
MEDICAL CARE
IN DIABETES—2020

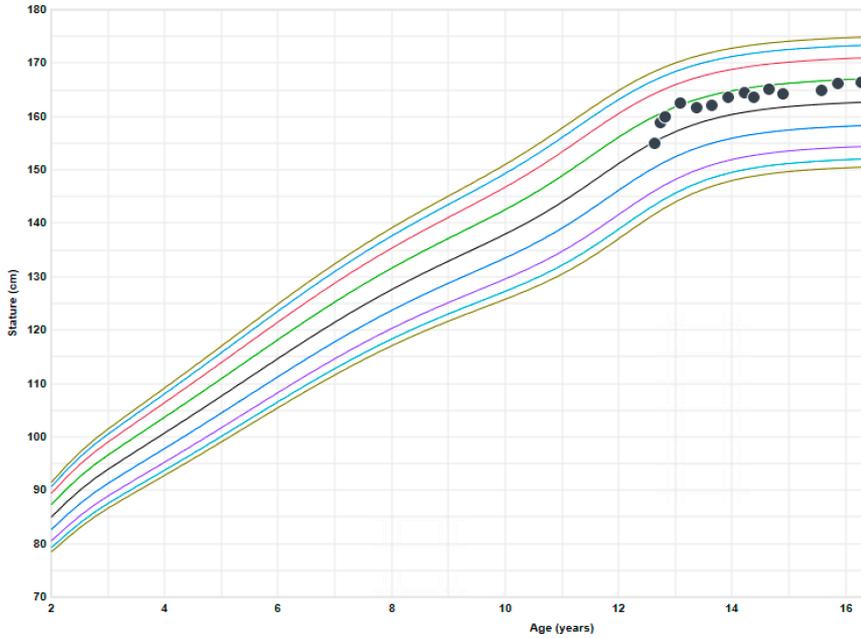
- 16 yo F with T1D who who presents for an elevated heart rate
- She states she first felt that something was wrong in mid-September when she was taught how to take a resting heart rate in health class and hers was 140. She confirmed this with her nurse who referred her to the pediatrician's office.
- She endorses jitteriness, shakiness and palpitations.
- She has not noticed a significant change in weight.
- 2 episodes of diarrhea a week ago with mild abdominal cramping.
- She has a history of intermittent headaches but they seem to be worse lately.
- She is an honors student and now finds it difficult to concentrate.



Growth Chart

Length Weight-for-length Weight BMI

Stature-for-age Percentiles (Girls, 2 to 20 years)

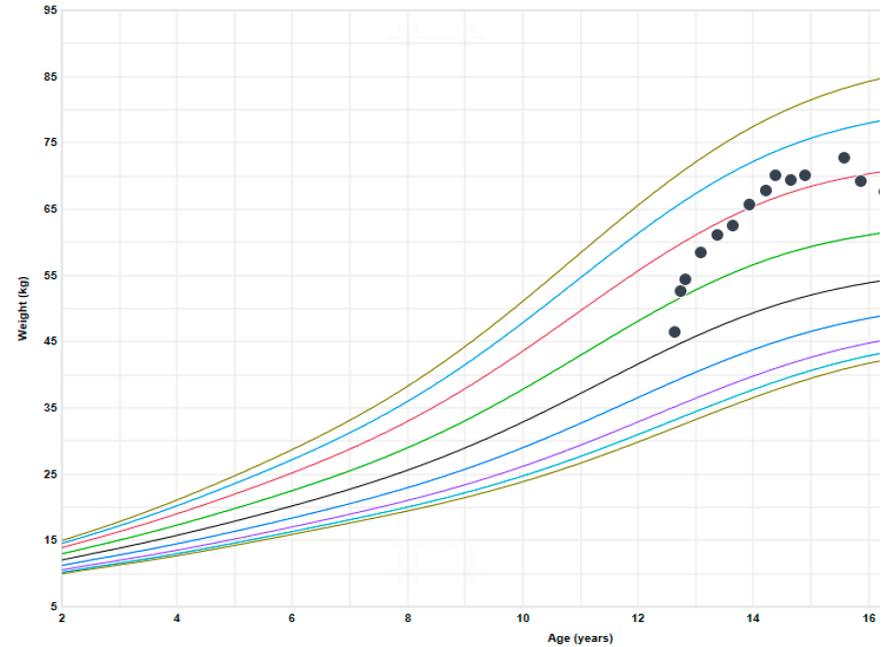


Source: Cent

Growth Chart

Length Weight-for-length Weight BMI

Weight-for-age Percentiles (Girls, 2 to 20 years)



PHYSICAL EXAM:

Vitals:

10/19/18 1353

BP: (!) 139/71
 Pulse: (!) 112
 Temp: 98.1 °F (36.7 °C)

GEN: healthy appearing girl with no dysmorphic features

HEENT: Normocephalic, PERRLA, EOMI, no lid lag or exophthalmos, oropharynx clear, dentition is normal. Neck is supple, + **thyromegaly**, thyroid gland about 1.5-2x larger than normal, no nodules appreciated

CV: Heart has regular rhythm and without murmurs, tachycardic to ~100

RESP: Lungs are clear to auscultation bilaterally

GI: soft, NT/ND, no organomegaly.

NEURO: Neurological exam is non-focal. DTR 2+. No resting tremor

SKIN: Skin and hair are normal.

2 years ago:

- TSH - 0.66 (0.5-4.3)
- FT4 - 0.8 (0.8-1.4)

Now

- **TSH - 0.01** (0.5-4.3)
- **FT4 - 2.7** (0.8-1.4)
- **Total T3 - 315** (86-192)
- **TSI - 544%** (<140%)
- **Thyroglobulin Ab - 9** (<4)
- TPO <15

- Hemoglobin A1c 9.5% (down from 10.7% 5 months earlier)

Diagnosis: Autoimmune hyperthyroidism

Treatment: Methimazole 10mg twice daily and Atenolol