Diabetic Ketoacidosis in Children

Objectives:

- Review pathogenesis, clinical manifestations and treatment of type one diabetes in children.

- Review diagnosis, management and prevention of diabetic ketoacidosis.

Definition:

- Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both.

Classification:

- **Type 1 diabetes :**

- **Type 2 diabetes:**

- **Other specific types:**

  - specific genetically defined forms of diabetes.

  - diabetes associated with other diseases or drug use.

Diagnosis:

- FPG ≥ 126 mg/dL

or

- Random PG ≥ 200 mg/dL + symptoms of diabetes

or

- 2hr PG in a 75-g OGTT ≥ 200 mg/dL

Genetics:

- Familial clustering of T1DM:
  - monozygotic twins 30-65%
  - dizygotic twins 6-10%
  - siblings 6%
  - mother 2%
  - father 7%

- Monogenic Type 1 Diabetes Mellitus: Rare
  ex. IPEX syndrome and APS

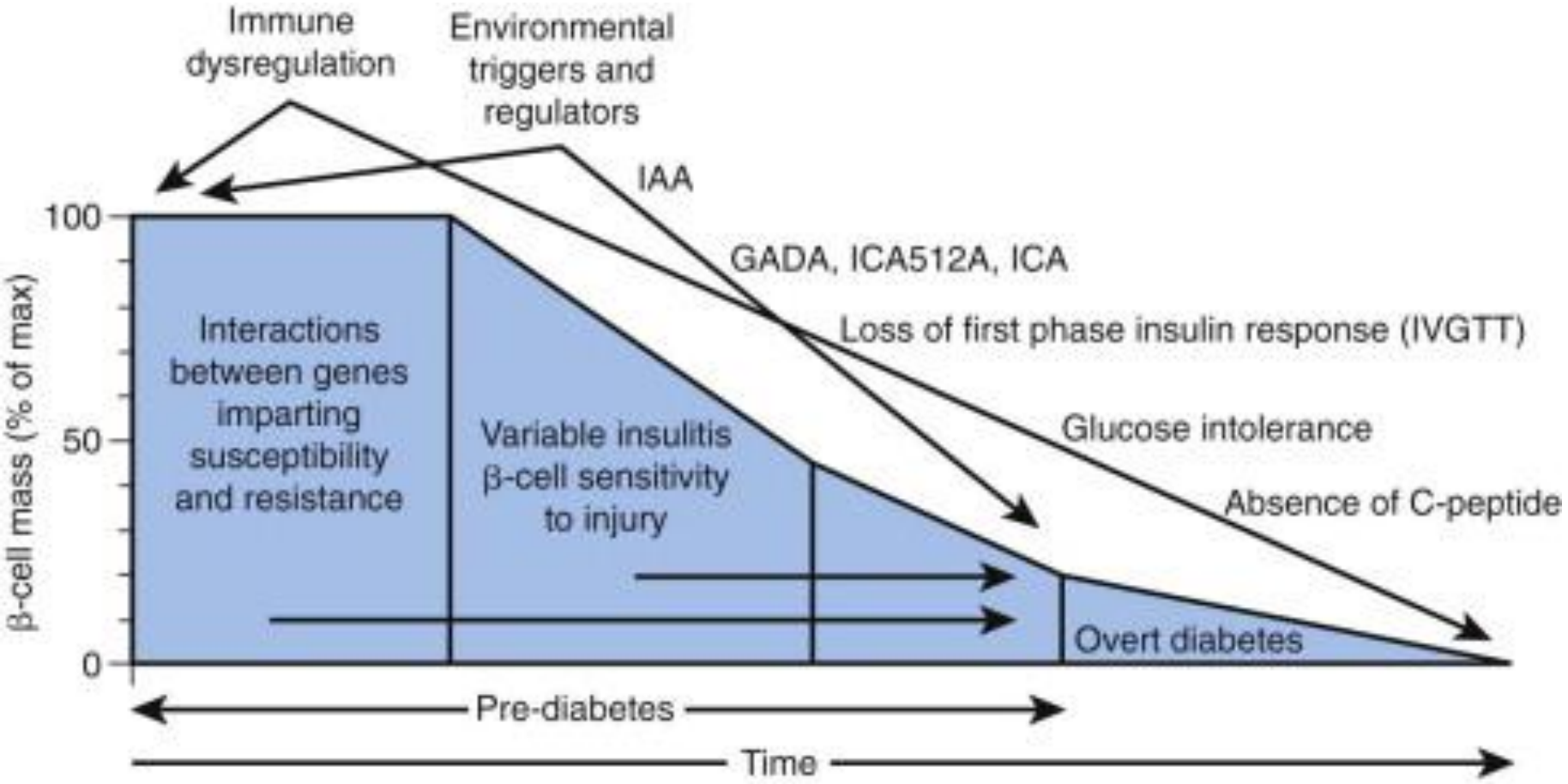
GENETIC DEFECTS OF **β-CELL FUNCTION**
Maturity-Onset Diabetes of Youth

- Onset 9-25 yr,
- AD inheritance
- A primary defect in insulin secretion.
- Diagnostic Criteria:
  - Diabetes in at least 3 generations with AD
  - Diagnosis before age 25 yr in at least 1 affected subject.

Environmental Factors:

- ~ 50% of monozygotic twins are discordant for T1DM.
- Variation in urban and rural areas populated by the same ethnic group.
- Change in incidence with migration.
- Increase in incidence in almost all populations in the last few decades.

Pathogenesis of type 1 diabetes :



Insulin

- Secreted by beta cells of pancreas
- Inhibits glycogenolysis and gluconeogenesis in liver
- Stimulates protein synthesis and lipogenesis
- Inhibits lipolysis and proteinolysis

Endogenous Insulin Profile

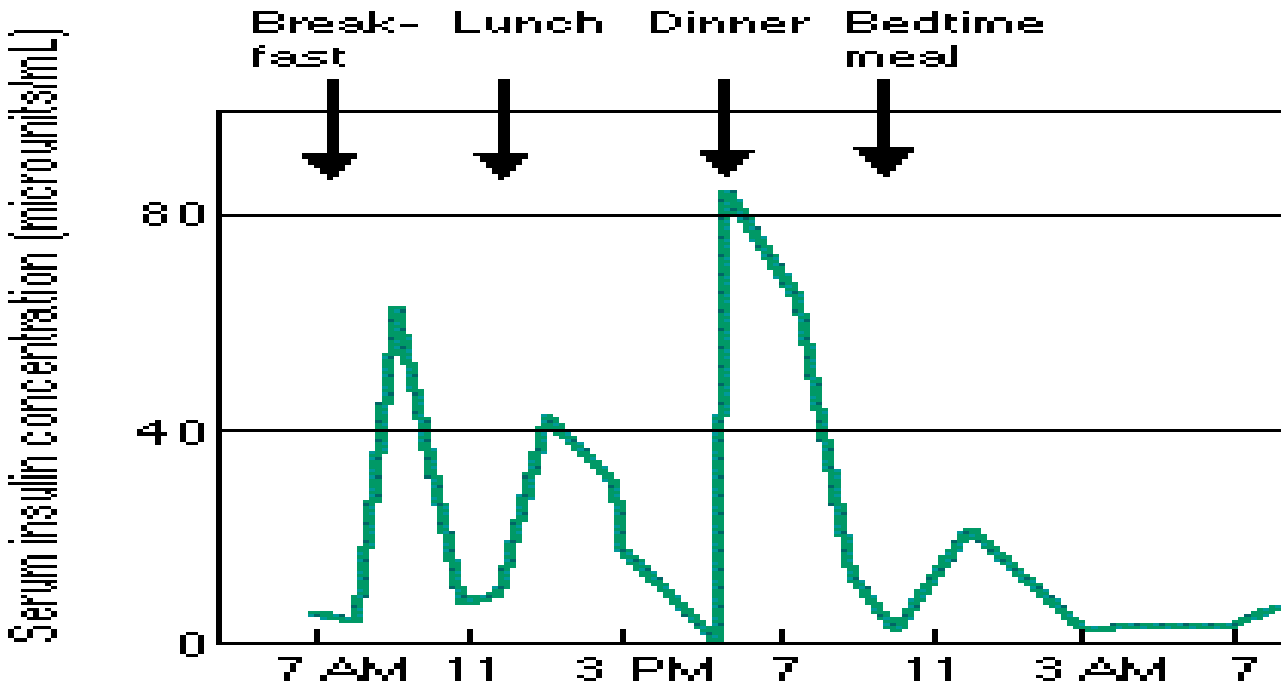


Figure 1. Normal insulin secretion. In the stimulated phase, serum insulin levels increase from within a few minutes before to 30 minutes after a meal. Return to basal level occurs within 2 hours.

Adapted from Galloway and Chance (5).

Galloway et al Horm Metab Res 1994

Absence of Insulin

- ⇓ lipogenesis + ⇑ lipolysis
- ⇓ protein synthesis + ⇑ proteinolysis
- ⇑ glycogenolysis + ⇑ gluconeogenesis

Counter-regulatory Hormones:						
	↓ insulin secretion	↓insulin action	↑Glycog-enolysis	↑Glucon-eogenesis	↑Lipolysis, ketogenesis	↓ glucose utilization
Epinephrine	+	+	+	+	+	+
Cortisol		+	+	+	+	+
GH		+	+	+	+	+
Glucagon			+	+	+	

Clinical Manifestations:

- Polyuria, polydipsia, polyphagia
- weight loss
- Fatigability

- DKA as first presentation.

- Progression may be accelerated by intercurrent illness or stress.

Diabetic Ketoacidosis

- The end result of the metabolic abnormalities resulting from a severe deficiency of insulin.

- DKA is 100% preventable.

- Occurs due to:
  - Non compliance to insulin therapy
    or
  - Intercurrent illnesses not managed according to the sick day management guidelines.

DKA – History:

- Polyuria , polydipsia, weight loss
- Abdominal pain
- Vomiting
- Confusion
- Tiredness
- Difficulty breathing

DKA – Clinical signs:

- Kussmaul breathing
- Lethargy
- Dehydration
- Signs of infection

Diagnosis of DKA:

- Glucose > 200 mg/dL
- pH < 7.3
- Ketonuria or ketonemia
- Serum Bicarbonate < 18 mmol/L

DKA – Investigations:

- Capillary glucose STAT
- Venous blood – glucose, gases, electrolytes, urea, creatinine
- Ketones in urine or blood

Management of DKA with vascular decompensation:

- ABCs.
- Normal saline 10 mL/kg to expand vascular space.
- Decrease to 5-7 mL/kg/hr with KCl.
- Not to infuse $NaHCO_3$ except in certain circumstances.
- Continuous IV insulin infusion 0.1 units/kg/hr.
- Observation and monitoring.
- If acidosis is improving and BG < 270 mg/dL or falls > 90 mg/dL/hr → change IV to D5/Normal Saline with potassium and decrease insulin infusion rate.

Table 2. An alternative example of fluid volumes for the **subsequent phase of rehydration**

Body weight, kg	Maintenance	DKA: give maintenance + 5% of body weight/24 h	
	mL/24 h	mL/24 h	mL/h
4	325	530	22
5	405	650	27
6	485	790	33
7	570	920	38
8	640	1040	43
9	710	1160	48
10	780	1280	53
11	840	1390	58
12	890	1490	62
13	940	1590	66
14	990	1690	70
15	1030	1780	74
16	1070	1870	78
17	1120	1970	82
18	1150	2050	85
19	1190	2140	89
20	1230	2230	93
22	1300	2400	100
24	1360	2560	107
26	1430	2730	114
28	1490	2890	120
30	1560	3060	128
32	1620	3220	134
34	1680	3360	140
36	1730	3460	144
38	1790	3580	149
40	1850	3700	154
45	1980	3960	165
50	2100	4200	175
55	2210	4420	184
60	2320	4640	193
65	2410	4820	201
70	2500	5000	208
75	2590	5180	216
80	2690	5380	224

Frequency of DKA

At disease onset

There is wide geographic variation in the frequency of DKA at onset of diabetes; rates inversely correlate with the regional incidence of type 1 diabetes. Frequencies range from approximately 15–70% in Europe and North America (23, 33–38). DKA at diagnosis is more common in younger children (<2 yr of age), often the consequence of diagnostic error or delayed treatment (39–41), those from ethnic minority groups, and in children whose families do not have ready access to medical care for social or economic reasons (20, 23, 37, 39, 42, 43).

In children with established diabetes

The risk of DKA in established type 1 diabetes is 1–10% per patient per year (3, 44–48):

Risk is increased in (47):

- Children who omit insulin (46).
- Children with poor metabolic control or previous episodes of DKA.
- Gastroenteritis with persistent vomiting and inability to maintain hydration.
- Children with psychiatric disorders, including those with eating disorders.
- Children with difficult or unstable family circumstances (e.g., parental abuse).
- Peripubertal and adolescent girls.
- Children with limited access to medical services.
- Insulin pump therapy (as only rapid- or short-acting insulin is used in pumps, interruption of insulin delivery for any reason rapidly leads to insulin deficiency) (3, 49).

Complications of DKA

- Arrhythmias/cardiac arrest – 2° to electrolyte abnormalities or possibly long QTc
- Venous thrombosis 2° hypercoagulable state
- Pulmonary edema/ARDS
- Acute renal failure (ATN)
- Bowel ischemia – necrosis, stricture formation

Pathophysiology of DKA-related cerebral edema

- Previous hypothesis assumed that fluid shifts caused by osmotic changes were central to DKA-related cerebral edema

- This assumption has not been well supported by clinical data

- Cerebral edema during DKA may be predominantly vasogenic and may result from activation of cell membrane ion transporters in the brain

Risks factors for CE

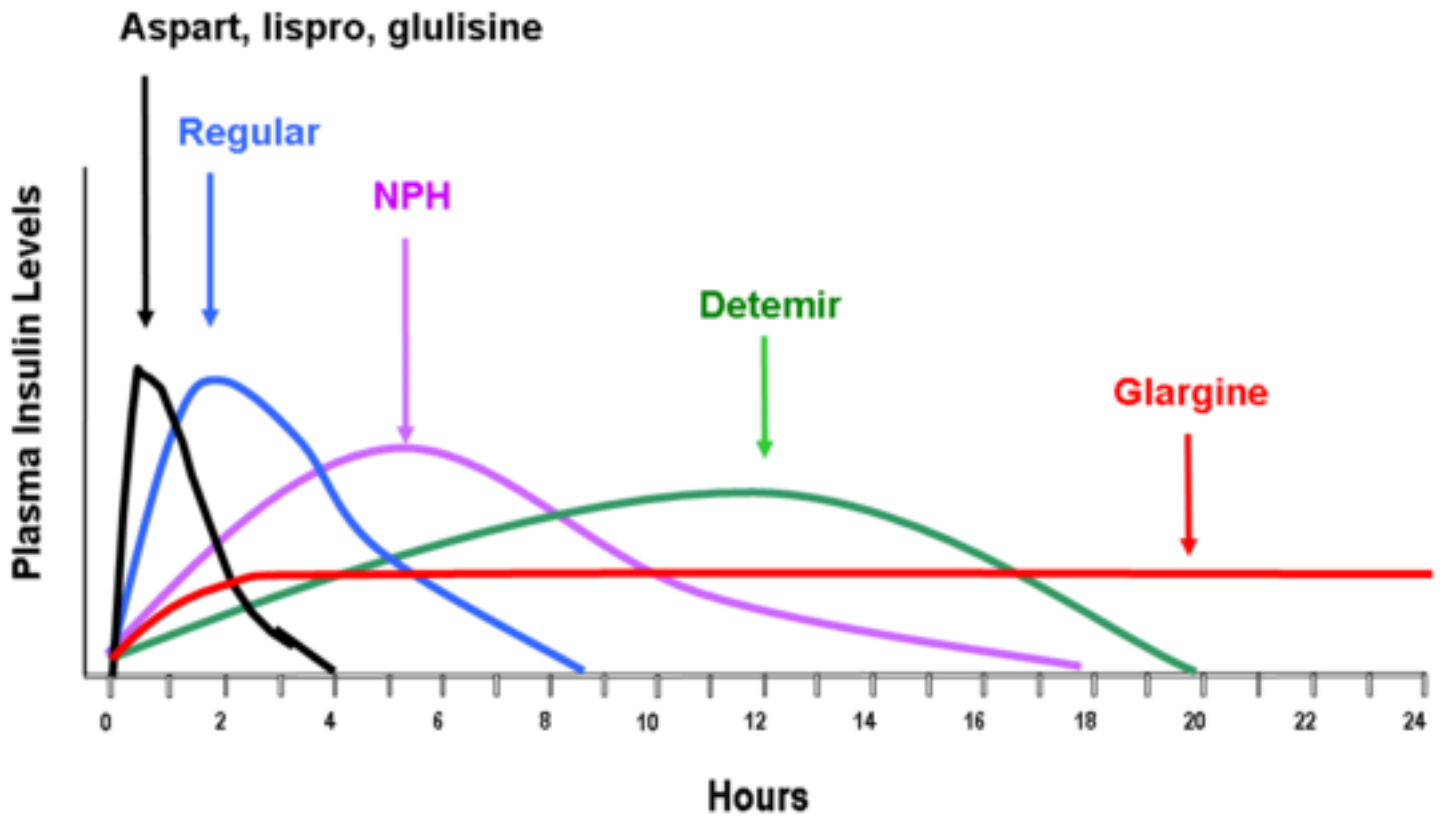
- Younger age (<5 years)
- New-onset diabetes
- High initial serum urea
- Low initial partial pressure of arterial CO2
- Rapid administration of hypotonic fluids
- IV bolus of insulin
- Early IV insulin infusion (within first hour of administration of fluids)
- Use of bicarbonate

Strategies to prevent Diabetic Ketoacidosis

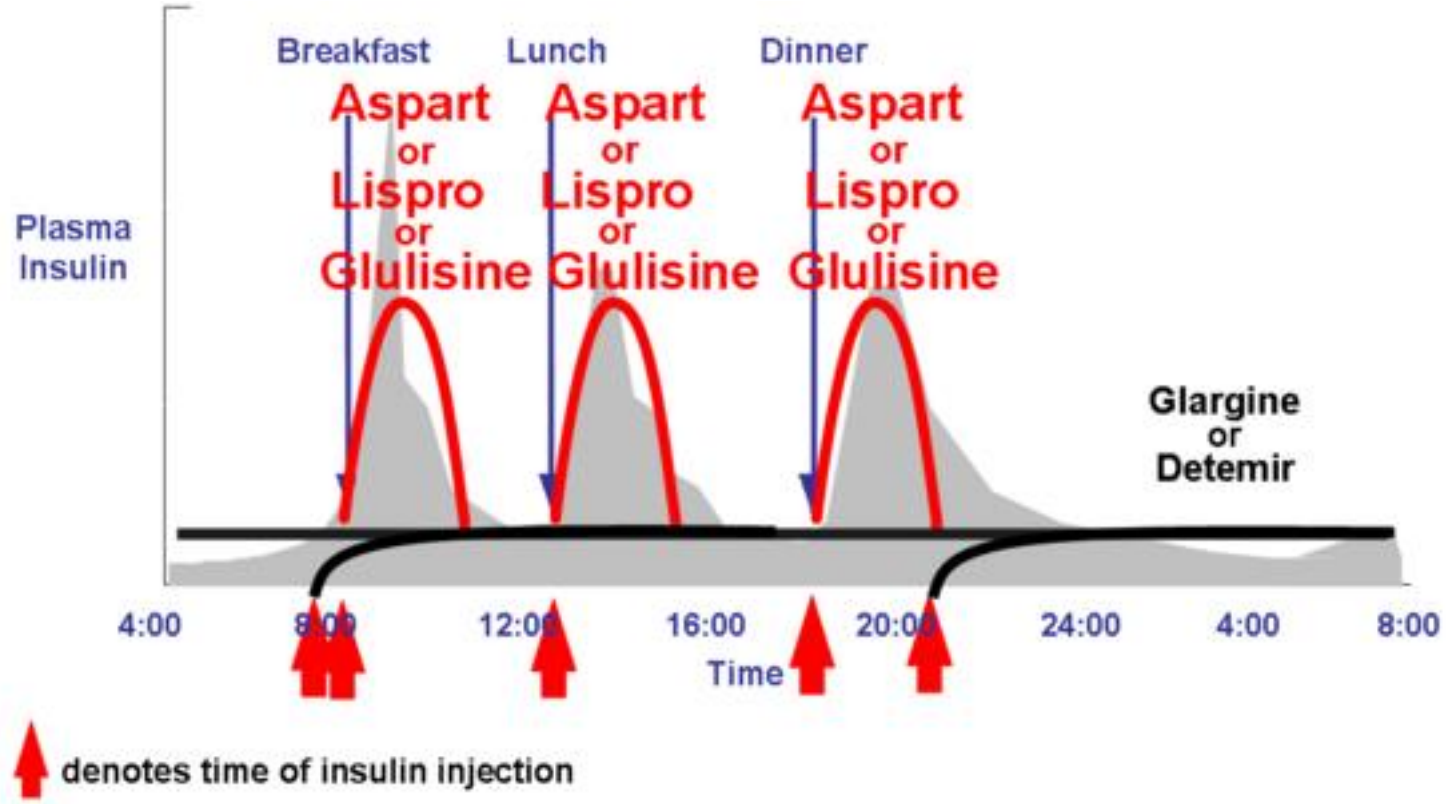
- To raise public awareness about symptoms and signs of diabetes.

- Beyond diagnosis:
  - Comprehensive diabetes education programs
  - Mental health intervention
  - Home monitoring of ketones or beta-hydroxybutyrate

Idealized insulin time-action profiles



Long **and Rapid- acting insulin**



Hypoglycemia

Symptoms of Low Blood Sugar Include:

- Hunger
- Trembling
- Sweating
- Extreme Mood changes
- Extreme tiredness
- Pale
- Dizziness
- Blurred Vision
- Headaches

Hypoglycemia

- These symptoms will always preceede NEUROGLYCOPENIA except in long standing type 1 diabetes/hypoglycemia unawareness.

- Action : confirm blood sugar is less than 72 mg/dL and TREAT WITH CARBOHYDRATE

Hypoglycemia

- Make sure the family has GLUCAGON and knows how to use it

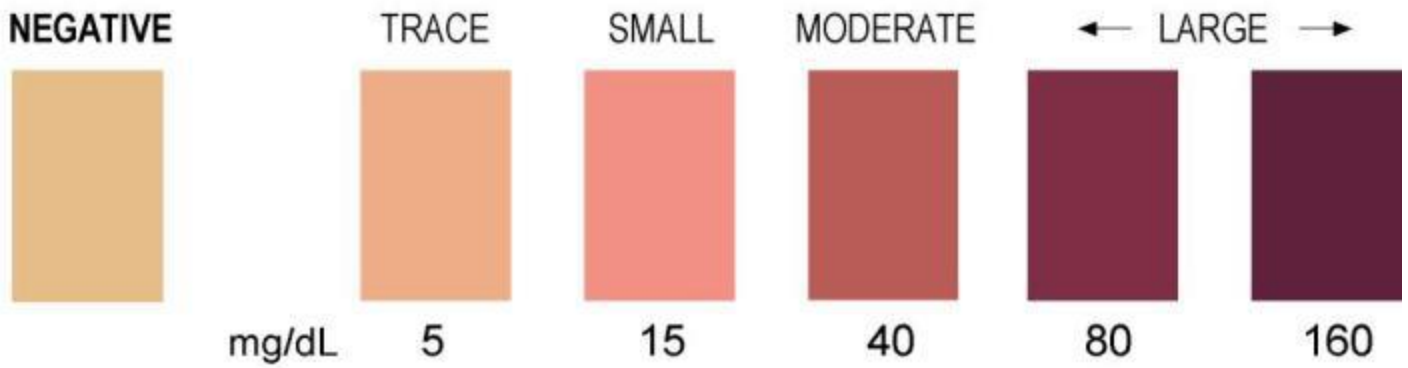
Sick Day Management

- Counter-regulatory hormones blunt insulin action and elevate glucose levels.
- Frequent blood glucose and ketone monitoring with adjustment of insulin doses.
- The overall goals are to maintain hydration, control glucose levels, and avoid ketoacidosis.
- **DO NOT OMIT INSULIN.**

Intercurrent Illness

- Check ketones EARLY
  - Always test when nausea or vomiting
  - Urine ketodiastix
  - Precision Xtra meter: Earlier detection, no need to collect urine

KETONE-Read at exactly **15 seconds.**



Comorbid Conditions:

- **Autoimmune thyroid disease**

  - 15-30% of individuals with type 1 diabetes .

- **Celiac disease:**

  - 4 to 9% of children with type 1 diabetes.
  - 60 to 70% are asymptomatic.

- **Addison disease:**

  - rare.

Diabetes Complications:

- **Nephropathy**

- **Retinopathy:**

The risk after 15 yr duration of diabetes:

- 98% T1DM
- 78% T2DM.

- **Neuropathy:**

The risk after 20 yr duration of diabetes:

- 20-30% T1DM
- 15-20% T2DM

- **Dyslipidemia**

- **Hypertension**

Up to 16% of adolescents with type 1 diabetes

ISPAD guidelines for retinopathy and nephropathy screening:

- Annually from age 11 years with after 2 years duration

And

- from 9 years with 5 years duration

THANK YOU