Hypoglycemia

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Hypoglycemia

Hypoglycemia is a clinical syndrome with diverse causes in which low plasma glucose concentrations lead to symptoms and signs, and there is resolution of the symptoms/signs when the plasma glucose concentration is raised .

Hypoglycemia

In patients with Diabetes, hypoglycemia is defined as : All episodes of an abnormally low plasma glucose concentration (with or without symptoms) that expose the individual to harm.

The diagnosis of hypoglycemia is not based on an absolute blood glucose level; it requires fulfillment of the *Whipple triad*:

I) Signs and symptoms consistent with hypoglycemia

2) Associated low glucose level

3) Relief of symptoms with supplemental glucose

- People with diabetes should become concerned about the possibility of hypoglycemia at a self-monitored blood glucose (SMBG) level ≤70 mg/dL **(3.9 mmol/L)**.

- This cut-off value has been debated, with some favoring a value of <63 mg/dL **(3.5 mmol/L)**.

Epidemiology

Hypoglycemia is common in type 1 diabetes, especially in patients receiving intensive therapy, in whom the risk of severe hypoglycemia is increased more than three fold.

Epidemiology

They suffer an average of *two episodes* of symptomatic hypoglycemia *per week*,

thousands of such episodes over a lifetime of diabetes, and

one episode of severe, at least temporarily disabling hypoglycemia *per year*.

Incidence :

- 3.14% in the intensive treatment group 1.03% in the standard group
- Increased risk among women, African Americans, those with less than high school education, aged participants .

For non diabetic people

For Non Diabetic patients
Glucose value < 50 mg/dl **(2.8mmo/L)**

Hypoglycemia
Facts

The brain relies almost exclusively on glucose

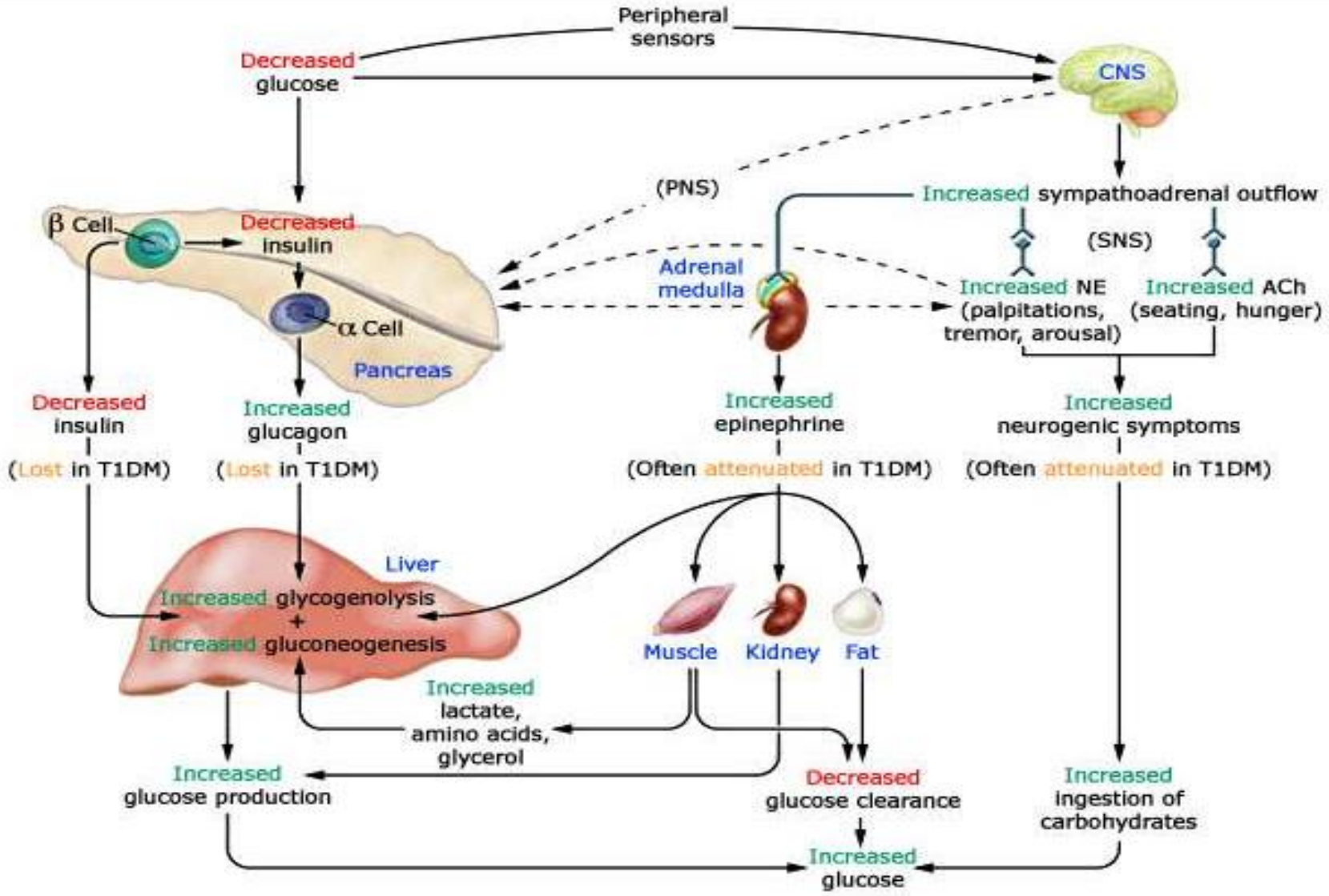
So …

Adequate uptake of glucose from the plasma is essential for normal brain function and survival

Luckily …

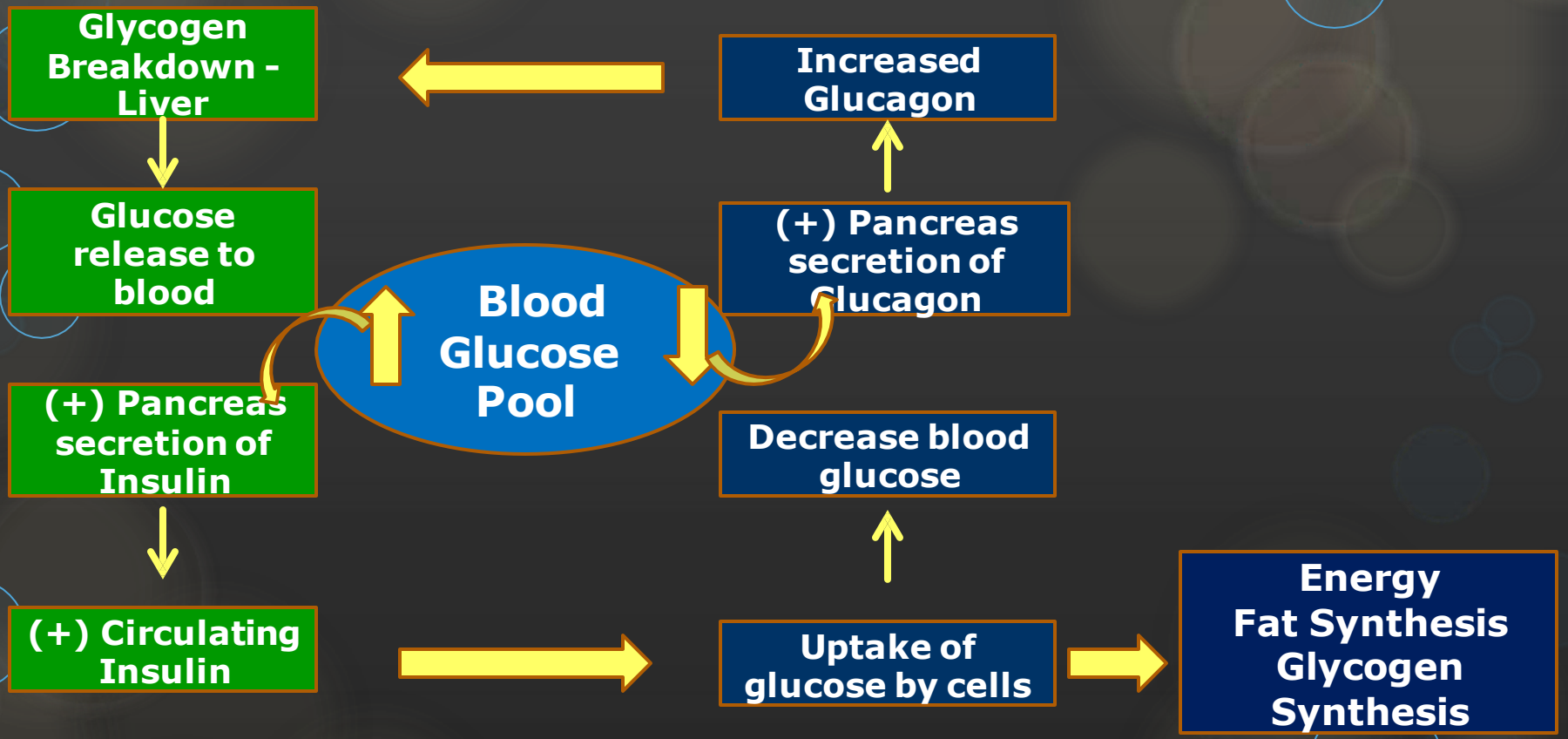
Very effective physiological and behavioral mechanisms normally prevent or rapidly correct hypoglycemia

Physiological and behavioral defenses against hypoglycemia



Decrements in insulin and increments in glucagon are lost and increments in epinephrine and neurogenic symptoms are often attenuated in insulin-deficient - T1DM and advanced T2DM.

Hypoglycemia – Patho-physiology



Hypoglycemia

Counter-regulatory Hormones

Plasma glucose Response	
65-70 mg/dl (3.6-3.9 mmol/L)	+ Glucagon and Epinephrine
60-65 mg/dl (3.3-3.6 mmol/L)	+ GH
<60 mg/dl (3.3 mmol/L)	+ Cortisol

Counterregulatory response to hypoglycemia

Condition	Glucose	Insulin	Glucagon	Epinephrine
Nondiabetic	↓	Decreases	Increases	Increases
T1DM	↓	No Decrease*	No Increase*	Attenuated Increase*•
T2DM				
Early	↓	Decreases	Increases	Increases
Late (Absolute endogenous insulin deficient)	↓	No Decrease*	No Increase*	Attenuated Increase*•

Iatrogenic hypoglycemia is the result of the interplay of absolute or relative therapeutic insulin excess and compromised physiological and behavioral defenses against falling plasma glucose concentrations in type 1 diabetes mellitus (T1DM) and advanced type 2 diabetes mellitus (T2DM).

* Defective glucose counterregulation.

• Hypoglycemia unawareness.

Courtesy of Dr. Philip Cryer.

Hypoglycemia
Clinical classification

Severe hypoglycemia = **Requiring assistance**

Documented symptomatic hypoglycemia =
Symptoms + plasma glucose ≤70 mg/dL **(3.9 mmol/L)**

Asymptomatic hypoglycemia…Unawareness
No typical symptoms but…
Plasma glucose ≤70 mg/dL **(3.9 mmol/L)**

Hypoglycemia
Clinical classification

Probable symptomatic hypoglycemia
Typical symptoms without plasma glucose determination (presumed)

Relative hypoglycemia :
Typical symptoms but with
Plasma glucose > 70 mg/dL (3.9 mmol

Hypoglycemia : S & S

Neuro-glycopenic

Plasma Glucose < 50 mg/dL (2.8 mmol/L)

Slurred speech

Cognitive impairment **Inattention and confusion**

Focal neurologic deficits **Seizures**

Behavioral/ Irritability/ Sudden moodiness

Change in personality **Lack of coordination**

Severe and prolonged hypoglycemia

LOC/Coma

Hypoglycemia
it matters …

The major limiting factor for achieving strict control in DM patients

Still , it is an expected price for adequate control

Hypoglycemia
it matters …

Bad impact on:

Quality of life: Fear / Psych

Satisfaction

Compliance; to diet and Rx

Achieving proper targets ?

Hypoglycemia
it matters …

Disturbing S & S

-Anxiety / Embarrassment
-Risk of accidents with impaired LOC
-Limitation of performance
-Rebound /Reaction
-Weight gain ?

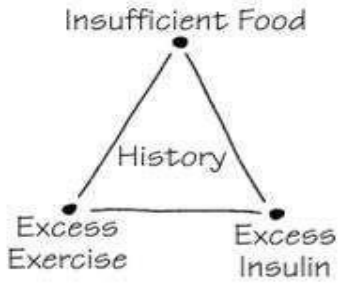
Hypoglycemia
…is common

Common ; up to 30- 60% in DM patients

Type 1 > Type 2 …But !

Intensive DM control (lower HbA1c…?)
Elderly
Duration of disease

Hypoglycemia : Setting / Causes



Onset
Rapid...
1 - 3 Hours

- Anxious
- Sweaty
- Hungry
- Confused
- Blurred or Double Vision
- Shaky
- Irritable
- Cool, Clammy Skin

Needs...
BLOOD SUGAR
Increased

Classification of symptoms of hypoglycaemia by age[1]

CHILDREN (pre-pubertal)	ADULTS	ELDERLY
Autonomic/ neuroglycopenic	Autonomic	Autonomic
	Neuroglycopenic	Neuroglycopenic
Behavioural	Non-specific malaise	Neurological
		Visual disturbances Incoordination Impaired balance

1. McAulay *et al. Diabet Med* 2001;18:690–705

Morbidity of hypoglycaemia in diabetes

Brain

Blackouts, seizures, coma

Cognitive dysfunction

Psychological effects

Cardiovascular

Myocardial ischaemia (angina and infarction)

Cardiac arrhythmias

Musculoskeletal

Falls, accidents (& driving accidents)

Fractures, dislocations

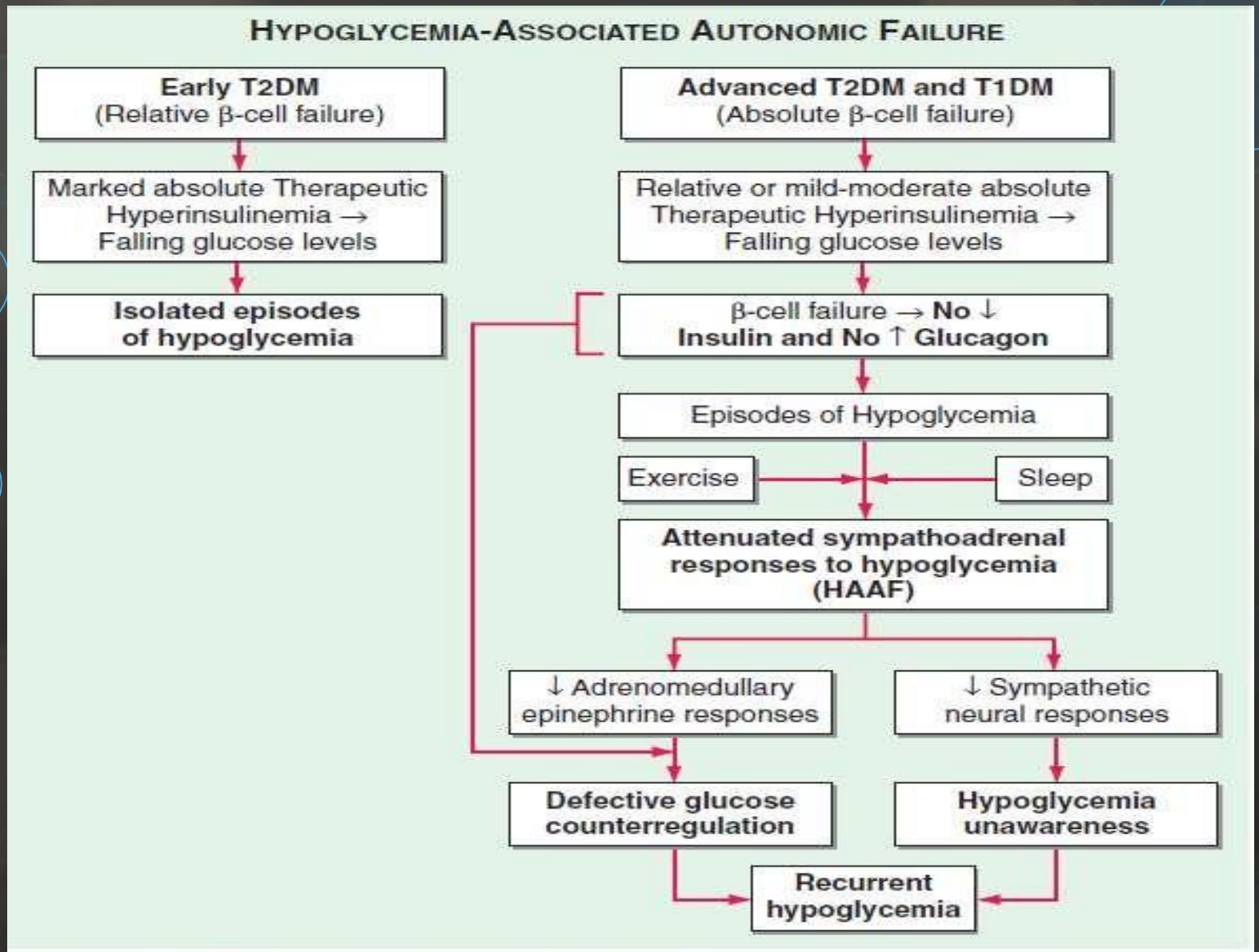


Figure 345-2 Hypoglycemia-associated autonomic failure in insulin-deficient diabetes.

Hypoglycaemic episodes often are unrecognised by patients

- Many episodes are asymptomatic; CGMS data show that unrecognised hypoglycaemia is common in people with insulin-treated diabetes
  - In one study, 63% of patients with T1D and 47% of patients with T2D had unrecognised hypoglycaemia as measured by CGMS (n=70)[1]

74% of all events occurred at night

  - In another study, 83% of hypoglycaemic episodes detected by CGMS were not detected by patients with T2D (n=31)[2]

54% of hypoglycaemic episodes were nocturnal, none of which were detected

CGMS, continuous glucose monitoring system

1. Chico *et al. Diabetes Care* 2003;26:1153–7; 2. Weber *et al. Exp Clin Endocrinol Diabetes* 2007;115:491–4

Setting for hypoglycemia

Identification of the precipitating factors
is important to prevent future events

Hypoglycemia
Setting

Common with

Diabetics who are treated with

Insulin releasing pills

(sulfonylureas, Meglitinides, or Nateglinide)

Insulin

Very unlikely with

Lifestyle changes (TLC) only

Using alone medications like :

(ex: Metformin ,DPP4I, GLP-1 + ,SGLT2 -)

Setting for hypoglycemia
Food intake

Skipped or delayed meals

Vomiting after meal & meds intake

Mismatch:
Wrong dose or too high a dose of medications for the amount of food; Too little carbohydrate

Setting for hypoglycemia

Unplanned / Excess exercise
without snack / Rx adjustment

Excessive insulin / OHA doses
Organ Failure Medications
Alcohol use

Identification of the precipitating factors is important to prevent future events

Hypoglycemia
Causes

Organ failure :

Renal
Hepatic
Cardiac

Endocrine Failure:

Adrenal
Glucagon
Cortisol
Pituitary
(ACTH/GH..)

Insulin excess -Absolute or relative

- Excess insulin (Secretagogues) Doses, ill-timed /wrong type
- Reduced exogenous glucose influx (Fasting /missed meals)
- Increased insulin-independent glucose utilization
  (During and shortly after exercise)
- Increased sensitivity to insulin (Hours after exercise, weight loss, nocturnal ,after improved contro

hypoglycemic unawareness

Longer duration of DM and Autonomic Neuropathy

The brain has a trigger point at which it leads to release stress hormones (Counter Regulatory Hormones)

With frequent low blood sugars, this set point gets reprogrammed to lower and lower blood sugar levels.

hypoglycemic unawareness

What causes hypoglycemic unawareness?

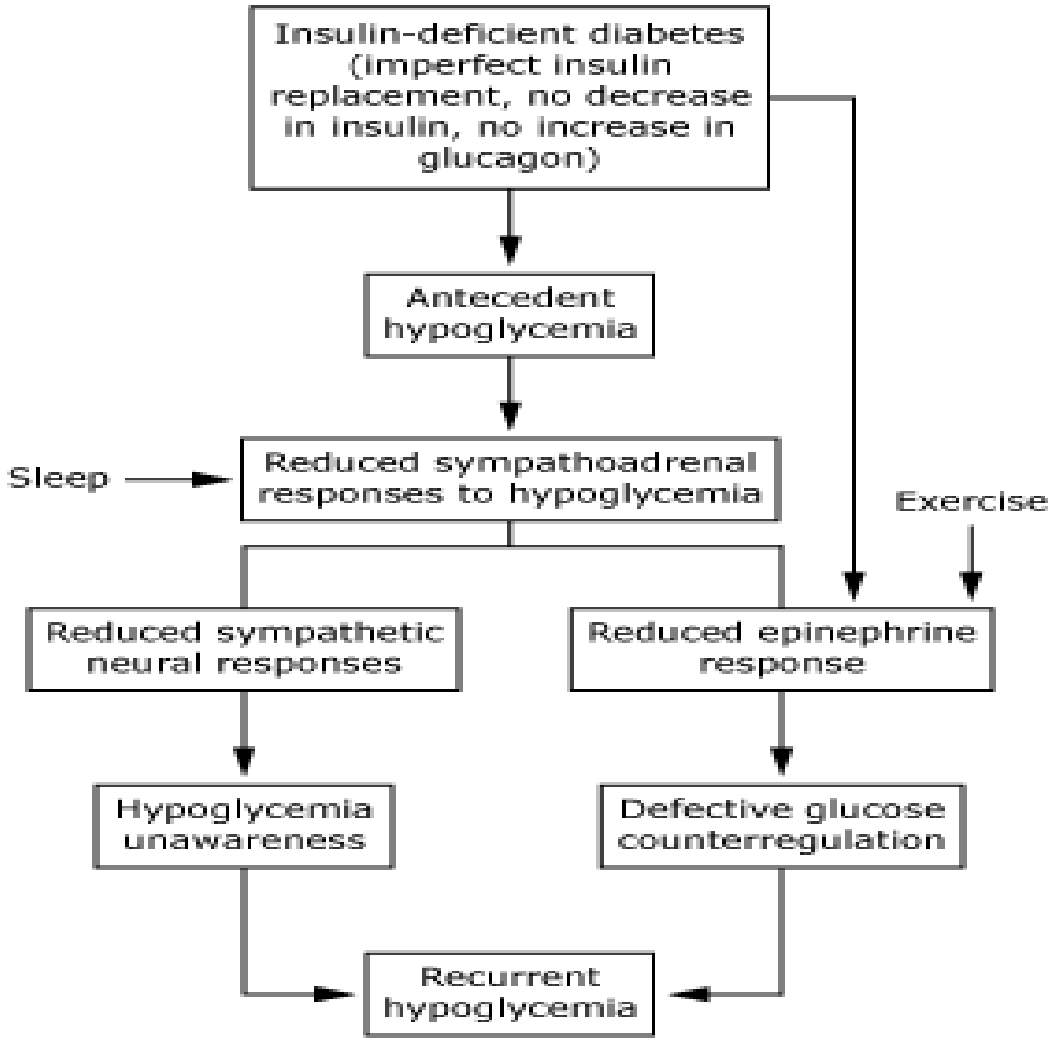
Loss of the ability to detect a low blood sugar

Patient needs to be vigilant; Do frequent monitoring

It may <u>not</u> be a permanent condition

Managed by easing the strict control for 2-3 weeks of more

Hypoglycemia-associated autonomic failure in diabetes



Modified from: Cryer PE. Diverse causes of hypoglycemia-associated autonomic failure in diabetes. N Engl J Med. 2004; 350:2272.

Hypoglycemia Management

Hypoglycemia
Management

Prevention = Education

Hypoglycemia-Prevention

- Patient education and empowerment
- Frequent self-monitoring of blood glucose (SMBG)
- Flexible and rational insulin (and other drug) regimens
- Individualized glycemic goals
- Professional guidance and support.

Hypoglycemia-Prevention

- Self-monitoring of blood glucose (SMBG)
- Keeping some sugar or sweet handy
- Teach patient/care-giver
- Medical alert identification
- Glucagon Emergency kit.

ADA-2015

Table 6.2—Summary of glycemic recommendations for nonpregnant adults with diabetes

A1C	<7.0%*
Preprandial capillary plasma glucose	80–130 mg/dL* (4.4–7.2 mmol/L)
Peak postprandial capillary plasma glucose†	<180 mg/dL* (<10.0 mmol/L)

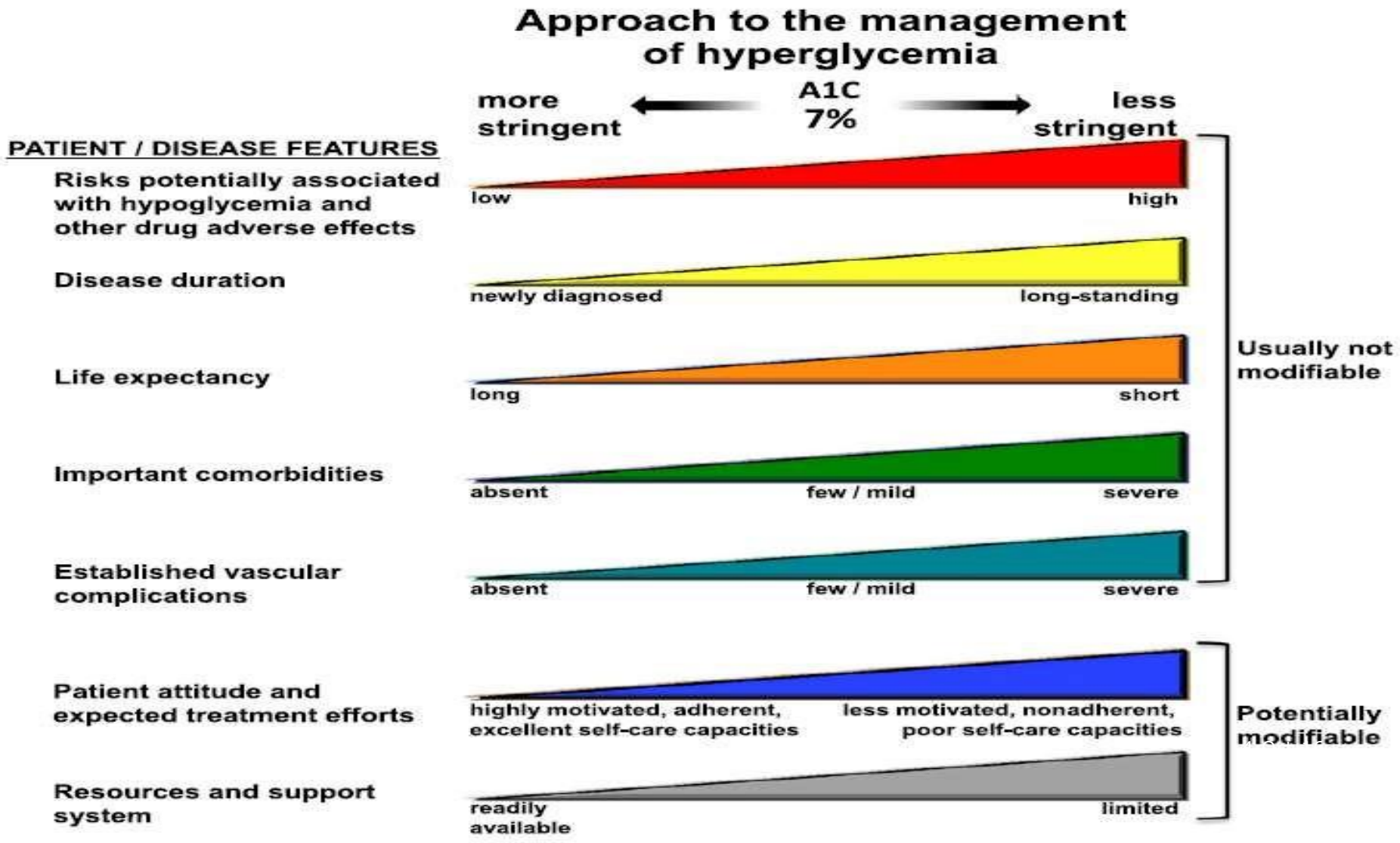
*More or less stringent glycemic goals may be appropriate for individual patients. Goals should be individualized based on duration of diabetes, age/life expectancy, comorbid conditions, known CVD or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations.

†Postprandial glucose may be targeted if A1C goals are not met despite reaching preprandial glucose goals. Postprandial glucose measurements should be made 1–2 h after the beginning of the meal, generally peak levels in patients with diabetes.

A1C Vs Average Glucose

A1C (%)	Mean plasma glucose mg/dl
6	~ 120
7	~ 150
8	~ 180
9	~ 210
10	~ 240
11	~ 270
12	~ 300

ADA – EASD Consensus:



Diabetes in Elderly

Table 1—*A framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes*

Patient characteristics/ health status	Rationale	Reasonable A1C goal (A lower goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden)	Fasting or preprandial glucose (mg/dL)	Bedtime glucose (mg/dL)	Blood pressure (mmHg)	Lipids
Healthy (Few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	**< 7.5 %**	90–130	90–150	<140/80	Statin unless contraindicated or not tolerated
Complex/intermediate (Multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild to moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	**< 8.0 %**	90–150	100–180	<140/80	Statin unless contraindicated or not tolerated
Very complex/poor health (Long-term care or end-stage chronic illnesses** or moderate to severe cognitive impairment or 2+ ADL dependencies)	Limited remaining life expectancy makes benefit uncertain	**< 8.5 %**	100–180	110–200	<150/90	Consider likelihood of benefit with statin (secondary prevention moreso than primary)

Hypoglycemia
Management

Recognize & Treat

Hypoglycemia
Recognition & Treatment

Recognize S & S

Document /Measure the glucose by finger stick
If < 70 mg/dl…

Conscious Vs Unconscious patient/ unable to swallow

Hypoglycemia
Treatment

Conscious patient

Rapidly absorbed CHO (glucose- or sucrose-containing foods) orally

Unconscious patient/ unable to swallow

IV dextrose or
IM glucagon

Hypoglycemia
Take control

+ve mild symptoms

Check blood sugar - Take fast acting CHO

½ cup of fruit juice or low fat / fat-free milk, Regular soda
3 glucose tablets
2 tbsp of raisins, 1 tbsp of honey or 2 tbsp of jam

About 15-20 grams of glucose

Hypoglycemia
Take control

+ve mild symptoms

You will need more glucose if the blood sugar is very low

Check your blood sugar again after 15 minutes.
Repeat same dose if the sugar is still low (<70mg/dl)

Double Dose if getting lower

Hypoglycemia
Take control

+ve severe symptoms :Call for help

Emergency IM glucagon by someone trained to do so

(SC/ IM injection) of 0.5 to **1.0 mg**

Recovery of consciousness within 10 to 15 minutes

Glucagon may cause nausea or vomiting

Check blood sugar

Don't wait for the emergency personnel arrival

Hypoglycemia
Take control

+ve severe symptoms
Patients in the hospital

Give 15-20 g of 50% glucose (dextrose) intravenously

A subsequent glucose infusion (or food, if patient is able to eat) is often needed, depending upon the cause of the hypoglycemia

ADA 2016 - Hypoglycemia

Individuals at risk for hypoglycemia should be asked about symptomatic and asymptomatic hypoglycemia at each encounter. C

Ongoing assessment of cognitive function is suggested with increased vigilance for hypoglycemia by the clinician, patient, and caregivers if low cognition and/or declining cognition is found. B

ADA 2016 - Hypoglycemia

Glucose (15–20 g) is the preferred treatment for the conscious individual with hypoglycemia, although any form of CHO that contains glucose may be used

15-minutes after treatment, if SMBG shows continued hypoglycemia, the treatment should be repeated.

Once SMBG returns to normal, the individual should consume a meal or snack to prevent recurrence of hypoglycemia. E

ADA 2015 - Hypoglycemia

Glucagon

Prescribe for all patients with increased risk of severe hypoglycemia

Keep it handy !!

Make sure about :

Proper storage /Refrigerator/ No direct light / Expiration date

ADA 2015 - Hypoglycemia

Glucagon

Caregivers or family members
(not limited to health care professionals)

Should be instructed on its proper mixing and administer immediately

Glucagon can cause vomiting
Risk of aspiration when unconscious
Keep patient on his side

ADA 2015 - Hypoglycemia

Hypoglycemia unawareness or
one or more episodes of severe hypoglycemia
should trigger reevaluation of the treatment regimen. E

Action:
Raise their glycemic targets
to avoid further hypoglycemia for at least several weeks
Aiming to partially reverse hypoglycemia unawareness
and reduce risk of future episodes. A

Hypoglycemia
Management

Address underlying cause
&
Intervene to prevent recurrence

Hypoglycemia
Management

Verify etiology & Prevent

Diet
Medication
Safe activities
Precautions : ID
Be equipped :CHO /Glucagon
.....
Educate …Educate …Educate

Hypoglycemia
Take home messages

All episodes of an abnormally low plasma glucose that expose the individual to harm) ;
PG <70 mg/dL (3.9 mmol/L)

Occurs in both type 1 DM and patients with type 2 DM
(Insulin and SU …highest risk)


Thanks