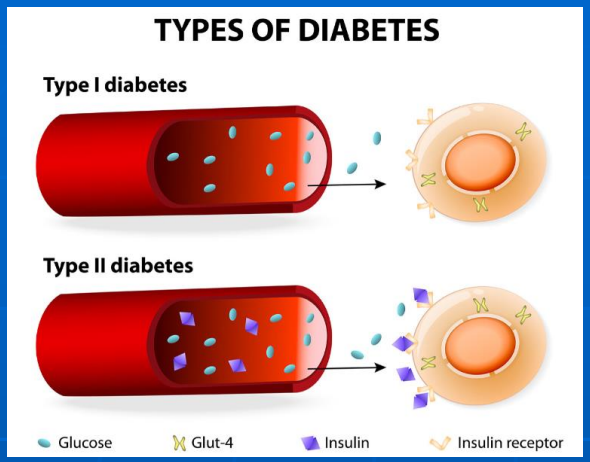
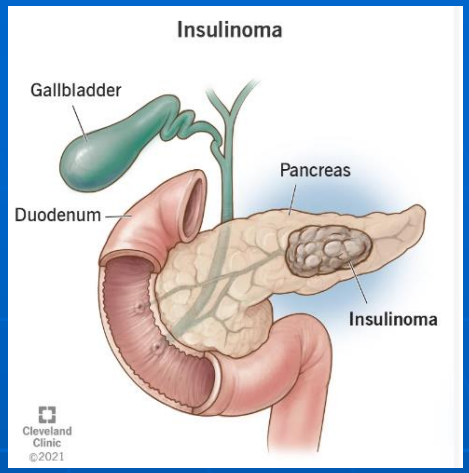




Hypoglycemia
Causes and management

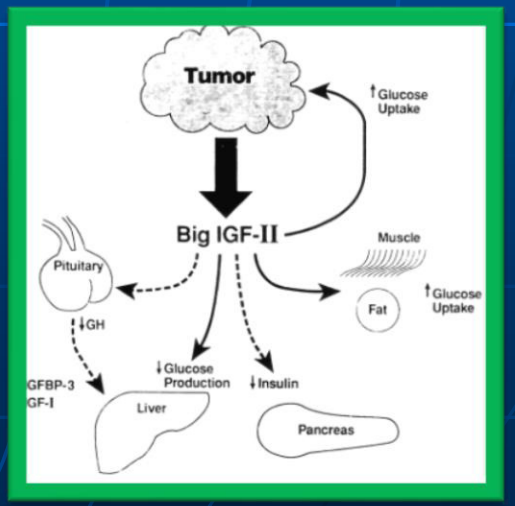
非胰島細胞腫瘤性低血糖 NICTH

Diagnosis of NICTH

- Fasting labs
- Low insulin, proinsulin, and c-peptide levels
- Elevated IGF-2 or Big IGF-2 levels
- IGF-2 and IGF-1 can be normal or low
- Elevated IGF-2: IGF-1 ratio is suggestive of the diagnosis

Cheng-Yi WANG

Jan. 05. 2024



OUTline

- INTRODUCTION
- PHYSIOLOGY INSULIN
- PATOPHYSIOLOGY
- DIAGNOSIS
- HIPOGLIKEMIA WITH AND WITHOUT DIABETES
- INSULINOMA
- CONCLUSION

Introduction: Metabolic emergency

WHAT IS METABOLIC EMERGENCIES?

Metabolic diseases can vary as much in clinical presentation as they can in classification, and neonates and infants frequently present with symptoms similar to those seen with other emergencies. Vomiting, alterations in neurologic status, and feeding difficulties are the most prominent features of metabolic emergencies.

Pediatric cases > Adult cases

It covers few aspects, including:

- Sodium
- Potassium
- Calcium
- Phosphate
- Magnesium
- Glucose
- Inborn Errors of Metabolism

- HYPOGLYCEMIA
- HYPONATREMIA
- INBORN ERRORS OF METABOLISM
- METABOLIC ACIDOSIS

Hypokalemia

Blood sugar < 50 mg/dl

HYPOGLYCEMIA

"Low plasma glucose level (<4.0 mmol/L)"

"Development of autonomic or neuroglycopenic symptoms in patients treated with insulin or OADs which are reversed by caloric intake."

低血糖

低血糖是指血液中--特別是血漿中--的葡萄糖濃度低於正常水平的現象，一般是治療糖尿病時的併發症，也可能是由多種原因所引起的，並導致一系列臨床的綜合病徵，就是低血糖症。低血糖可能會導致動作笨拙、說話困難、迷亂、神志喪失、癲癇或死亡，也可能會感覺到飢餓、流汗、顫抖或虛弱等症狀。通常低血糖的症狀會快速發作。 低血糖的常見病因為服用胰島素、磺醯脲類、雙胍類等治療糖尿病的藥物吃得比平時少、動得比平時多以及平...

Hypoglycemia, levels

Table 1—Summary of consensus definitions

Outcome	Definition
Hypoglycemia	Level 1: glucose <70 mg/dL (3.9 mmol/L) and glucose ≥54 mg/dL (3.0 mmol/L) Level 2: glucose <54 mg/dL (3.0 mmol/L) Level 3: a severe event characterized by altered mental and/or physical status requiring assistance
Hyperglycemia	Level 1—elevated glucose: glucose >180 mg/dL (10 mmol/L) and glucose ≤250 mg/dL (13.9 mmol/L) Level 2—very elevated glucose: glucose >250 mg/dL (13.9 mmol/L)
Time in range	Percentage of readings in the range of 70–180 mg/dL (3.9–10.0 mmol/L) per unit of time
DKA	Elevated serum or urine ketones (greater than the upper limit of the normal range) and serum bicarbonate <15 mmol/L or blood pH <7.3

(L1066, L1067)

Table 2—Levels of hypoglycemia

Level	Glycemic criteria/description
Level 1	Glucose <70 mg/dL (3.9 mmol/L) and glucose ≥54 mg/dL (3.0 mmol/L)
Level 2	Glucose <54 mg/dL (3.0 mmol/L)
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance

L1066, L1067

Control of Blood sugar in DM

Table 3—HbA_{1c} testing and time in range outcome

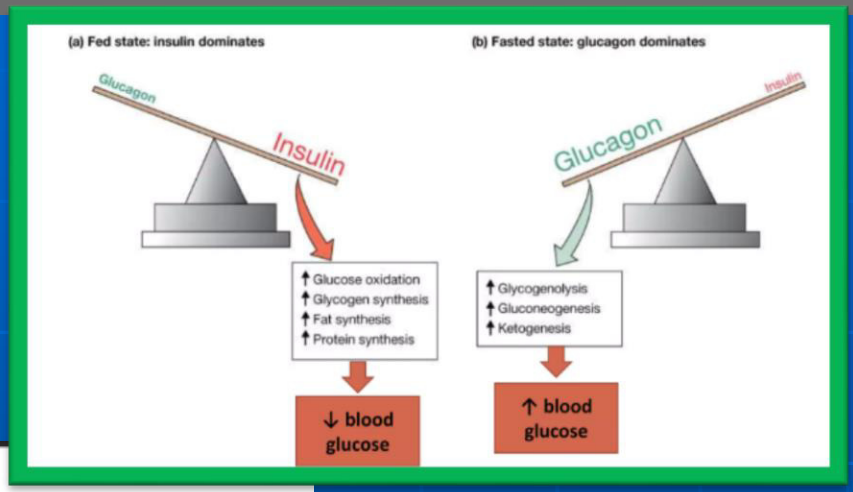
HbA_{1c} testing	Time in range outcome
Evaluates single HbA_{1c} levels	Evaluates continuous glucose levels
Compares HbA_{1c} levels 3 months apart	May compare fluctuations for any given amount of time
Does not capture hypoglycemic or hyperglycemic levels occurring in the same day	Captures all glucose levels for the given time frame and identifies time within a safe range
Less likely to capture impact of acute interventions	Likely to capture impact of acute interventions

More commonly, time in range has been adopted by researchers evaluating the precision and effectiveness of emerging glucose monitoring and automated insulin delivery technologies. None of these studies relate time in range to any long-term diabetes outcomes, as these studies are of short duration. In one example, researchers compared a wearable, bihormonal, automated device to an insulin pump for 5 days over a 96-h period in 52 adults and adolescents with type 1 diabetes. Researchers measured the percent time in range by the hour, and the **desired glucose range was defined as 70–180 mg/dL (3.9–10.0 mmol/L**). They demonstrated that the **bihormonal device was able to keep patients within a range of 70– 180 mg/dL (3.9–10.0 mmol/L) for more time than the insulin pump,** concluding that this device was a more effective means of managing blood glucose (65)

CONCLUSIONS

- The Steering Committee developed definitions for outcomes beyond HbA1c in type 1 diabetes including hypoglycemia, hyperglycemia, time in range, and DKA. These definitions were based on relevant published evidence and the clinical experience and expertise of the Steering Committee representatives and members of the Advisory Committees. 1628 Consensus Report Diabetes Care Volume 40, December 2017 Knowledge gaps, including around PROs, were identified and should be addressed by future research. The Steering Committee recommends use of the defined clinically meaningful outcomes beyond HbA1c in the research, development, and evaluation of type 1 diabetes therapies

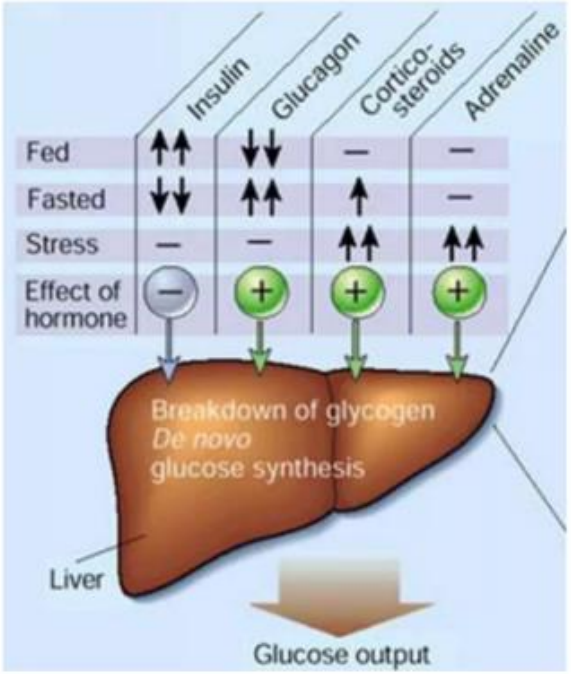
Glucose homeostasis

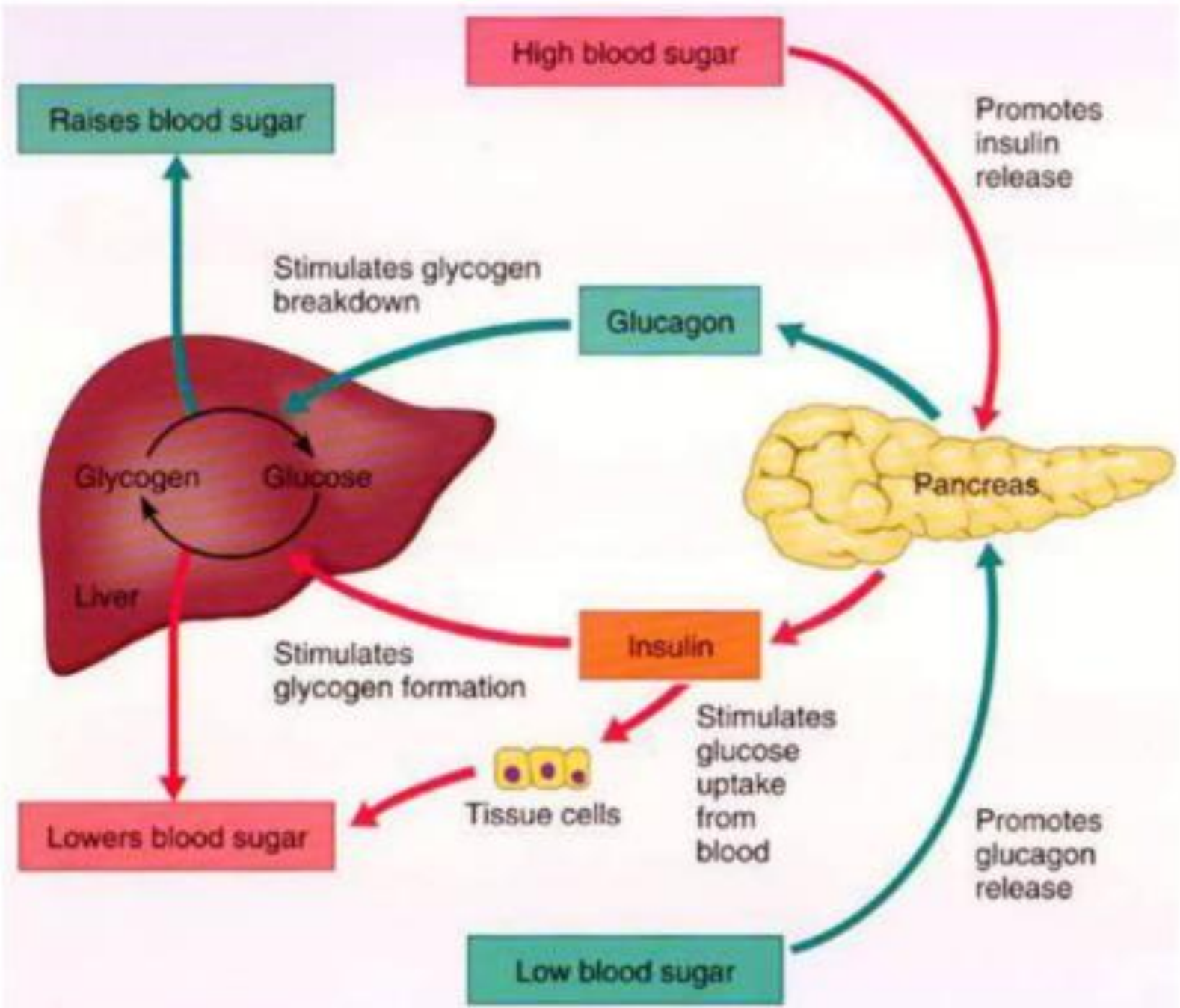


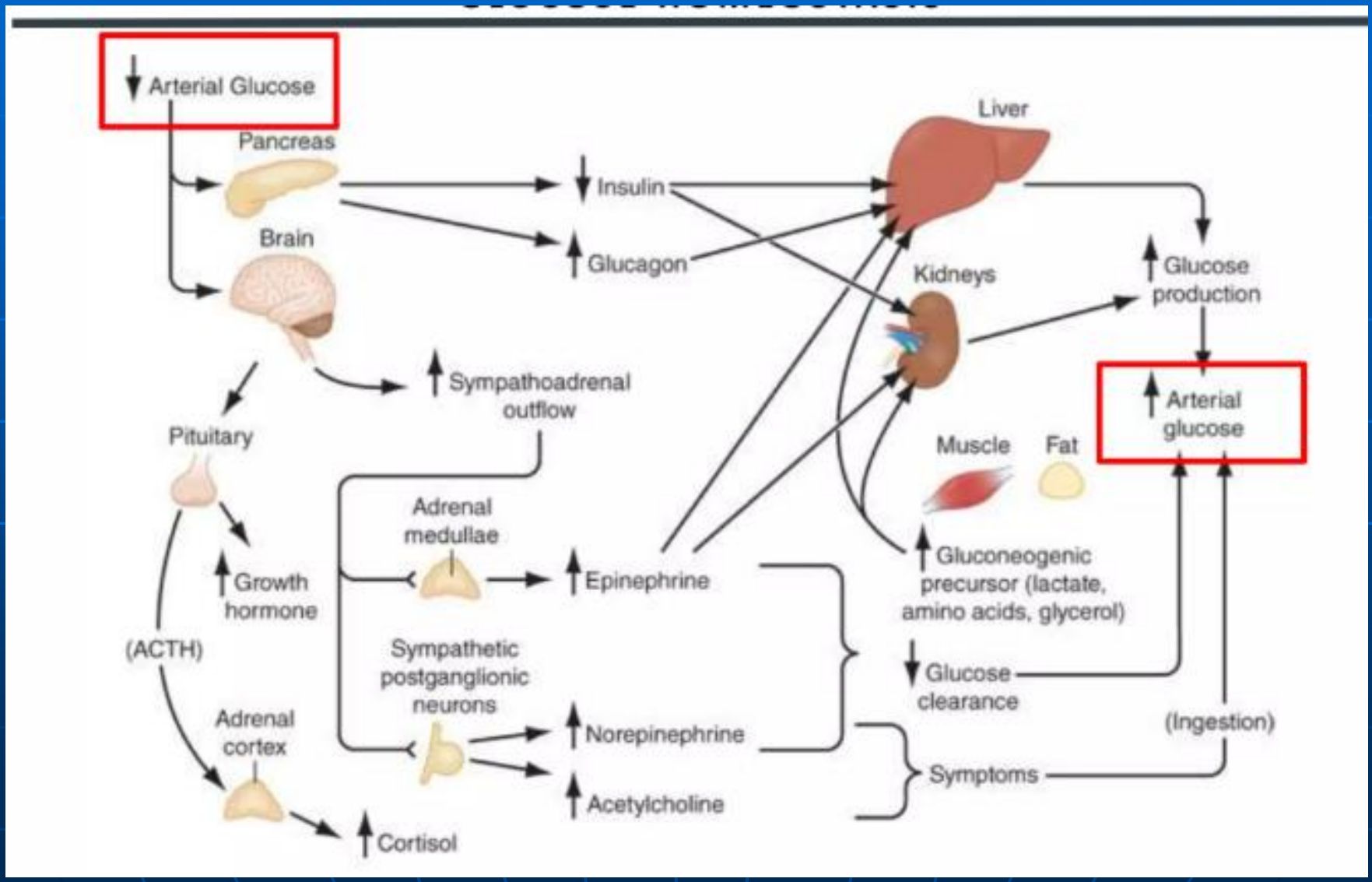
GLUCOSE HOMEOSTASIS

Two major hormones regulating glucose homeostasis are **insulin (beta cells)** and **glucagon (alpha cells)**. They work together to promote homeostasis of energy and metabolism of carbohydrates and fats. There are also other regulating hormones, such as somatostatin, epinephrine and cortisol.

High blood glucose → stimulates insulin release from pancreas → stimulates glucose uptake from blood into skeletal muscles and fat, stimulates glycogen formation in liver, inhibits release of glucagon




High blood sugar
Raises blood sugar
Promotes insulin release
Stimulates glycogen breakdown
Glucagon
Glycogen
Glucose
Liver
Pancreas
Insulin
Stimulates glycogen formation
Stimulates glucose uptake from blood
Tissue cells
Lowers blood sugar
Promotes glucagon release
Low blood sugar


Arterial Glucose
Pancreas
Insulin
Glucagon
Liver
Brain
Kidneys
Glucose production
Sympathoadrenal outflow
Arterial glucose
Pituitary
Muscle
Fat
Adrenal medullae
Growth hormone
Epinephrine
Gluconeogenic precursor (lactate, amino acids, glycerol)
(ACTH)
Sympathetic postganglionic neurons
Glucose clearance
Adrenal cortex
Norepinephrine
(Ingestion)
Symptoms
Acetylcholine
Cortisol

Effect of hypoglycemia-consciousness改變

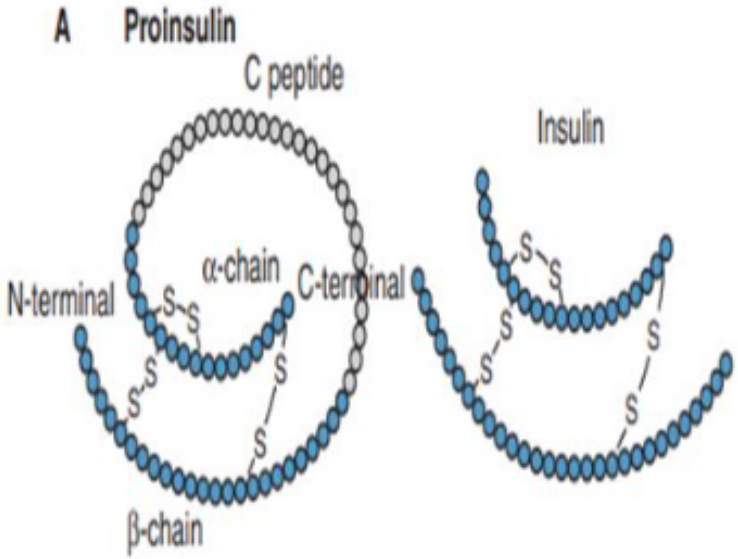
INTRODUCTION

- Hypoglycemia can cause serious morbidity
- if severe and prolonged, it can be fatal.
- It should be considered in any patient with episodes of confusion, an altered level of consciousness, or a seizure.

Insulin caused hypoglycemia

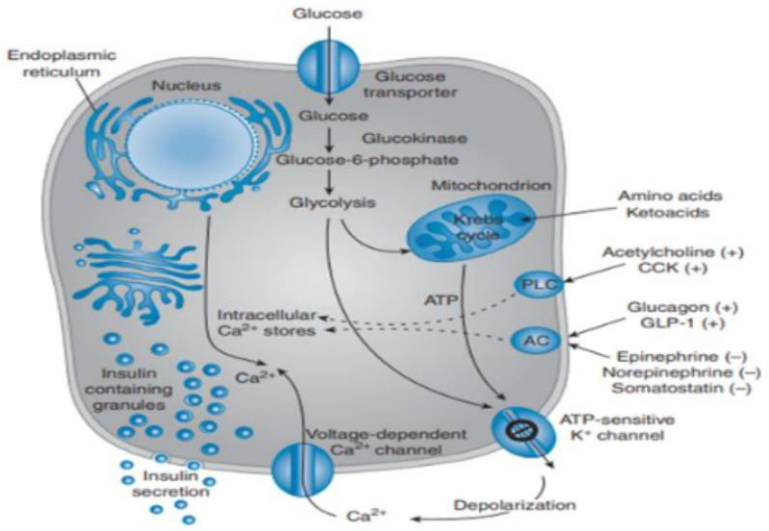
PHYSIOLOGY OF INSULIN

- Insulin is a peptide hormone synthesized from preproinsulin.
- The active form of insulin is produced by modification of proinsulin by cleavage of the C-peptide
- Both insulin and the cleaved C-peptide are packaged in secretory granules and are coreleased in response to glucose stimulation



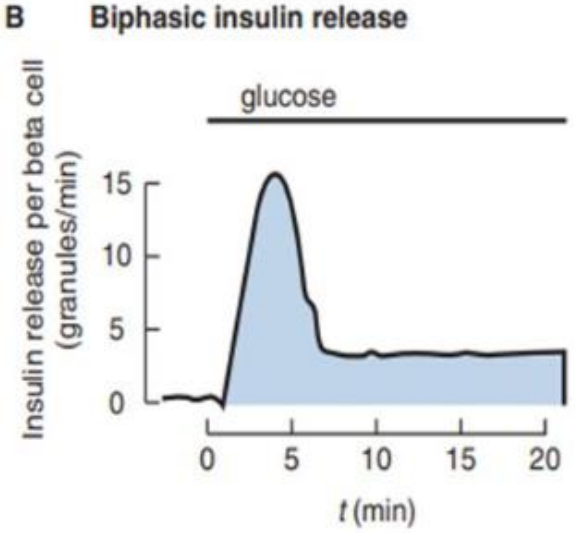
Molina, P. E. *Endocrine physiology*. M. H. Education. New York: Lange Medical Books/McGraw-Hill. Fourth Edition. 2013

Regulation of Insulin Release



Molina, P. E. *Endocrine physiology*. M. H. Education. New York: Lange Medical Books/McGraw-Hill. Fourth Edition. 2013

- Insulin release occurs in a biphasic mode.
- First phase of insulin → rapid release of ready insulin in the first 10 minutes
- Second phase → slowly released insulin in 24 hours



Insulin effects on carbohydrate, fat, and protein metabolism

Metabolic effects	Insulin stimulates	Insulin inhibits
Carbohydrate metabolism	Glucose transport in adipose tissue and muscle Rate of glycolysis in muscle and adipose tissue Glycogen synthesis in adipose tissue, muscle, and liver	Glycogen breakdown in muscle and liver Rate of glycogenolysis and gluconeogenesis in the liver
Lipid metabolism	Fatty acid and triacylglycerol synthesis in tissues Uptake of triglycerides from the blood into adipose tissue and muscle Rate of cholesterol synthesis in the liver	Lipolysis in adipose tissue, lowering the plasma fatty acid level Fatty acid oxidation in muscle and liver Ketogenesis
Protein metabolism	Amino acid transport into tissues Protein synthesis in muscle, adipose tissue, liver, and other tissues	Protein degradation in muscle Urea formation

Jameson, J. *Harrison's Endocrinology, 3E*. McGraw-Hill Education, 2013

Definitions of hypoglycemia

Table 2. Definitions of levels of hypoglycemia

Level 1	Glucose <70 mg/dL (3.9 mmol/L) and glucose ≥54 mg/dL (3.0 mmol/L). This level of hypoglycemia should alert patients that they may need to ingest carbohydrate to prevent progressive hypoglycemia.
Level 2	Glucose <54 mg/dL (3.0 mmol/L). This level of hypoglycemia is associated with increased risk for cognitive dysfunction and mortality.
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance. This level of hypoglycemia is life-threatening and requires emergent treatment typically with glucagon.

Source: Adapted from Agiostratidou, G, et al. *Diabetes Care*, 2017; 40(12): 1622–1630.

CAUSE OF HYPOGLYCEMIA IN ADULTS

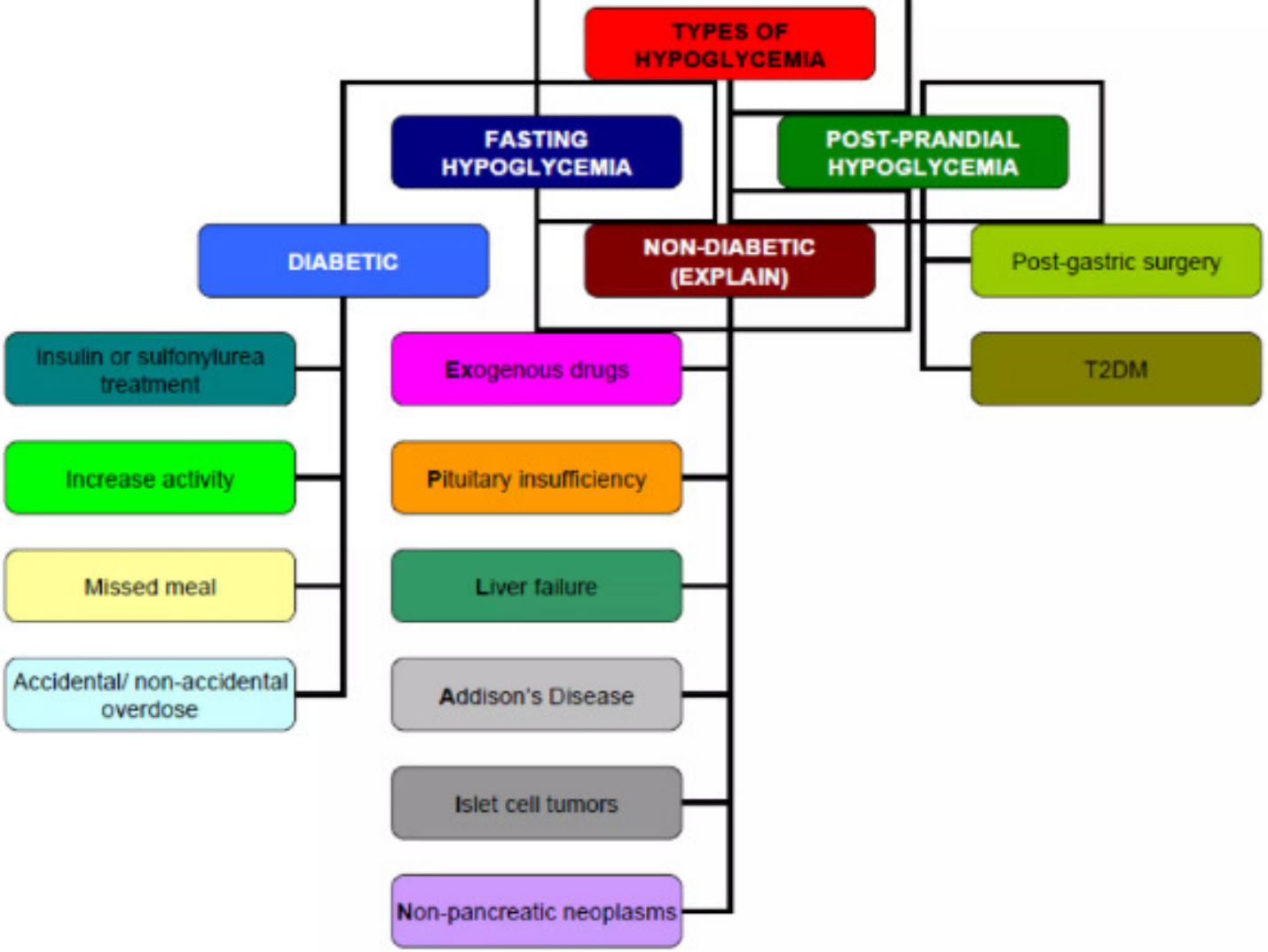
成人低血糖之原因

Ill or medicated individual
1. Drugs
   - Insulin or insulin secretagogue
   - Alcohol
   - Others
2. Critical illness
   - Hepatic, renal, or cardiac failure
   - Sepsis
   - Inanition
3. Hormone deficiency
   - Cortisol
   - Glucagon and epinephrine (in insulin-deficient diabetes)
4. Non–islet cell tumor

Seemingly well individual
5. Endogenous hyperinsulinism
   - Insulinoma
   - Functional beta-cell disorders (nesidioblastosis)
     - Noninsulinoma pancreatogenous hypoglycemia
     - Post–gastric bypass hypoglycemia
   - Insulin autoimmune hypoglycemia
     - Antibody to insulin
     - Antibody to insulin receptor
   - Insulin secretagogue
   - Other
6. Accidental, surreptitious, or malicious hypoglycemia

Jameson, J. *Harrison's Endocrinology, 3E*. McGraw-Hill Education, 2013

CLASSIFICATION



PREDISPOSING FACTORS

(risk factors)

HYPOGLYCEMIA

- Advancing age
- Poor health knowledge
- Hypoglycemia unawareness
- The most common cause of hypoglycemia is **medications used to treat diabetes mellitus such as insulin and sulfonylureas.** Long standing insulin therapy.
- **Risk is greater in diabetics who have eaten less than usual, exercised more than usual or have drunk alcohol.**
- Relative therapeutic insulin excess
  - ❑ Reduce oral intake, missed meals
  - ❑ Improve insulin sensitivity; eg. Increased physical activity, improved glycemic control, weight loss
- Low blood sugar may occur in otherwise healthy babies who have not eaten for a few hours.
- Other causes of hypoglycemia include **kidney failure**, certain tumors, such as **insulinoma**, **liver disease**, **hypothyroidism**, **starvation**, **inborn error of metabolism**, **severe infections**, **reactive hypoglycemia** and a number of **drugs** including **alcohol**.

Table 1. Individuals at high risk for developing hypoglycemia

- Individuals taking medications known to cause hypoglycemia (eg, insulin, sulfonylureas, meglitinides)
- Individuals with impaired kidney or liver function
- Older-age patients
- Preschool-age children
- Individuals with a history of severe hypoglycemia
- Individuals with cognitive impairment or intellectual disability that may reduce ability to respond to low blood glucose
- Individuals with impaired awareness of hypoglycemia
- Individuals with a longer duration of diabetes (including those using insulin for ≥5 y)
- Individuals who use alcohol
- Individuals with eating disorders
- Individuals with irregular eating schedules
- Individuals that are fasting for religious or cultural reasons
- Individuals with a history of untreated pituitary, adrenal, or thyroid insufficiency

Source: Adapted from American Diabetes Association Professional Practice Committee. *Diabetes Care*, 2022; 45(Suppl. 1): S46–S59.

L1093

GoaLS OF Diabetes CARE

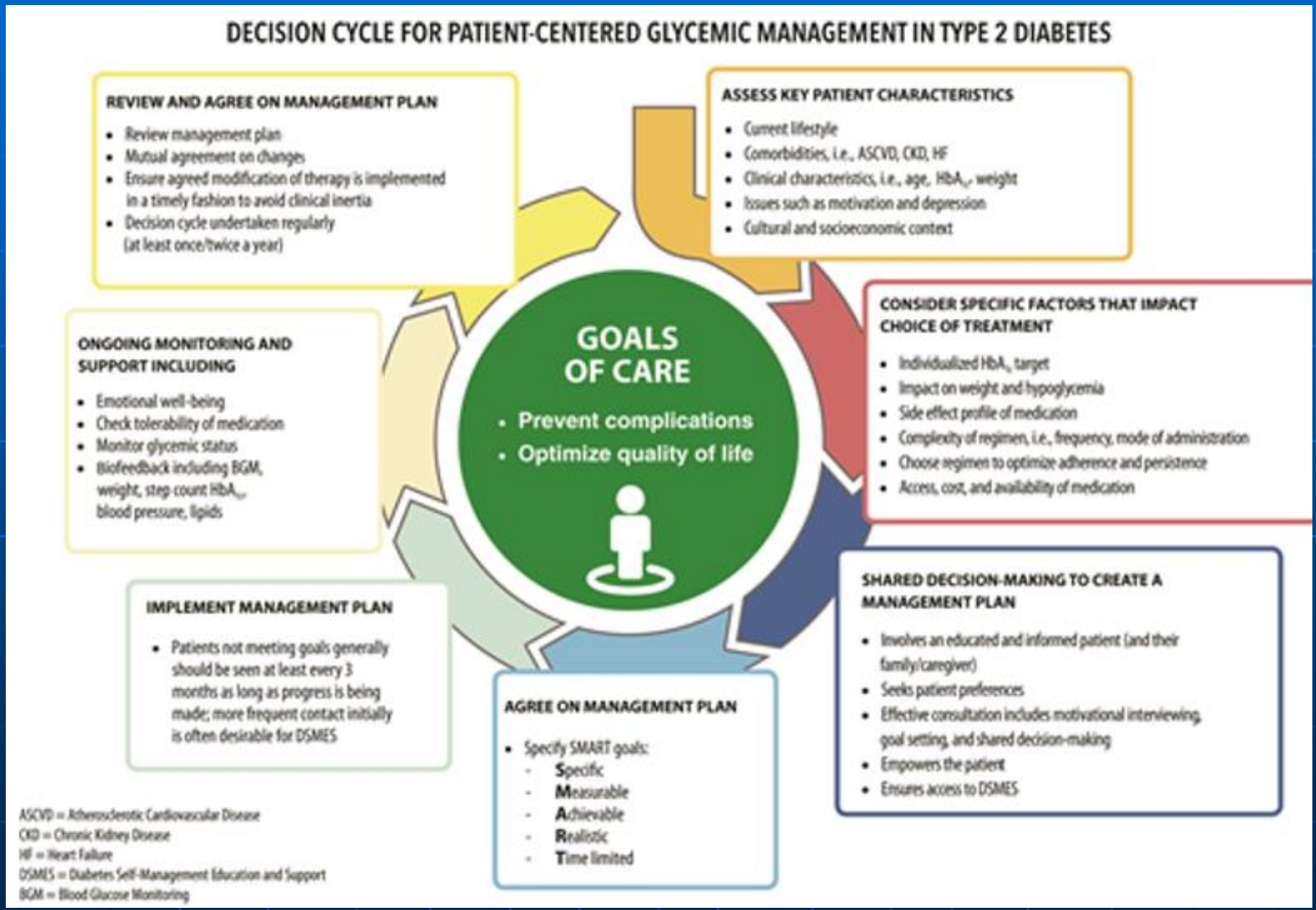


Table 4.1 - Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PAST MEDICAL AND FAMILY HISTORY	**Diabetes history**			
	• Characteristics at onset (e.g., age, symptoms)	✓		
	• Review of previous treatment regimens and response	✓		
	• Assess frequency/cause/severity of past hospitalizations	✓		
	Family history			
	• Family history of diabetes in a first-degree relative	✓		
	• Family history of autoimmune disorder	✓		
	Personal history of complications and common comorbidities			
	• Common comorbidities (e.g., obesity, OSA, NAFLD)	✓		✓
	• High blood pressure or abnormal lipids	✓		✓
	• Macrovascular and microvascular complications	✓		✓
	• Hypoglycemia: awareness/frequency/causes/timing of episodes	✓	✓	✓
	• Presence of hemoglobinopathies or anemias	✓		✓
	• Last dental visit	✓		✓
	• Last dilated eye exam	✓		✓
	• Visits to specialists	✓	✓	✓

確定診斷之後之生活習性

	Interval history			
	• Changes in medical/family history since last visit		✓	✓
BEHAVIORAL FACTORS	• Eating patterns and weight history	✓	✓	✓
	• Assess familiarity with carbohydrate counting (e.g., type 1 diabetes, type 2 diabetes treated with MDI)	✓		✓
	• Physical activity and sleep behaviors	✓	✓	✓
	• Tobacco, alcohol, and substance use	✓		✓

Physical evaluation

Table 4.1 (cont.)- Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits

		INITIAL VISIT	EVERY FOLLOW-UP VISIT	ANNUAL VISIT
PHYSICAL EXAMINATION	• Height, weight, and BMI; growth/pubertal development in children and adolescents	✓	✓	✓
	• Blood pressure determination	✓	✓	✓
	• Orthostatic blood pressure measures (when indicated)	✓		
	• Fundoscopic examination (refer to eye specialist)	✓		✓
	• Thyroid palpation	✓		✓
	• Skin examination (e.g., acanthosis nigricans, insulin injection or insertion sites, lipodystrophy)	✓	✓	✓
	• Comprehensive foot examination			
	• Visual inspection (e.g., skin integrity, callous formation, foot deformity or ulcer, toenails)**	✓		✓
	• Screen for PAD (pedal pulses—refer for ABI if diminished)	✓		✓
	• Determination of temperature, vibration or pinprick sensation, and 10-g monofilament exam	✓		✓
	• Screen for depression, anxiety, and disordered eating	✓		✓
	• Consider assessment for functional performance*	✓		✓
	• Consider assessment for functional performance*	✓		✓

Laboratory evaluation

LABORATORY EVALUATION	• A1C, if the results are not available within the past 3 months	✓	✓	✓
	• If not performed/available within the past year	✓		✓
	• Lipid profile, including total, LDL, and HDL cholesterol and triglycerides#	✓		✓^
	• Liver function tests#	✓		✓
	• Spot urinary albumin-to-creatinine ratio	✓		✓
	• Serum creatinine and estimated glomerular filtration rate*	✓		✓
	• Thyroid-stimulating hormone in patients with type 1 diabetes#	✓		✓
	• Vitamin B12 if on metformin	✓		✓
	• Serum potassium levels in patients on ACE inhibitors, ARBs, or diuretics+	✓		✓

ABI, ankle-brachial pressure index; ARBs, angiotensin receptor blockers; CGM, continuous glucose monitors; MDI, multiple daily injections; NAFLD, nonalcoholic fatty liver disease; OSA obstructive sleep apnea;PAD, peripheral arterial disease

*At 65 years of age or older

+May be needed more frequently in patients with known chronic kidney disease or with changes in medications that affect kidney function and serum potassium (see Table 11.1)

#May also need to be checked after initiation or dose changes of medications that affect these laboratory values (i.e., diabetes medications, blood pressure medications, cholesterol medications, or thyroid medications)

^In people without dyslipidemia and not on cholesterol-lowering therapy, testing may be less frequent

**Should be performed at every visit in patients with sensory loss, previous foot ulcers, or amputations

1. Confusion
   Loss of consciousness
2. Plapitationand tremor
3. Sweating and hunger
4. Symptoms resolved after glucose level is raised.
5. Heart rate an systolic pressure typically raised and may not be raised.

Clinical Manifestations

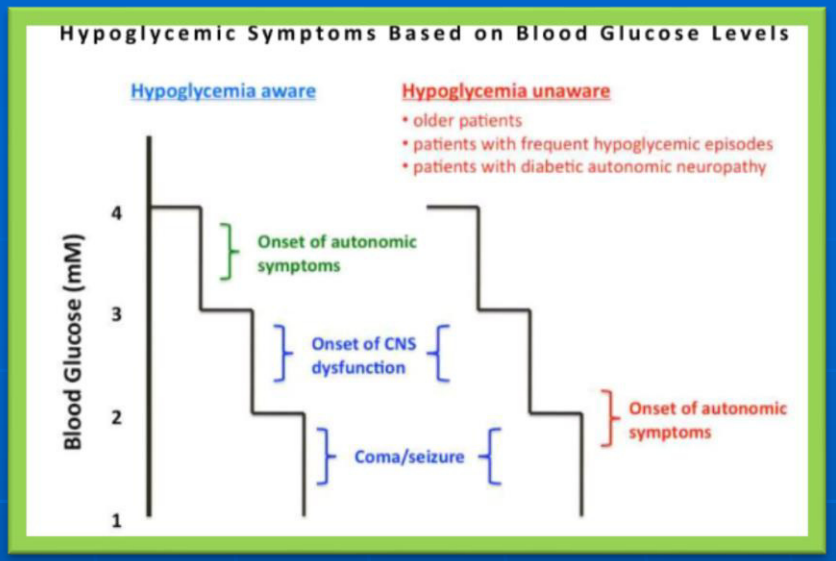
- Neuroglycopenic symptoms → behavioral changes, confusion, fatigue, seizure, loss of consciousness,
- Neurogenic (or autonomic) symptoms →palpitations, tremor, and anxiety
- cholinergic symptoms → sweating, hunger, and paresthesias
- low plasma glucose concentration and their resolution after the glucose level is raised (Whipple's triad)
- Heart rate and systolic blood pressure are typically increased but may not be raised in an individual who has experienced repeated, recent episodes of hypoglycemia

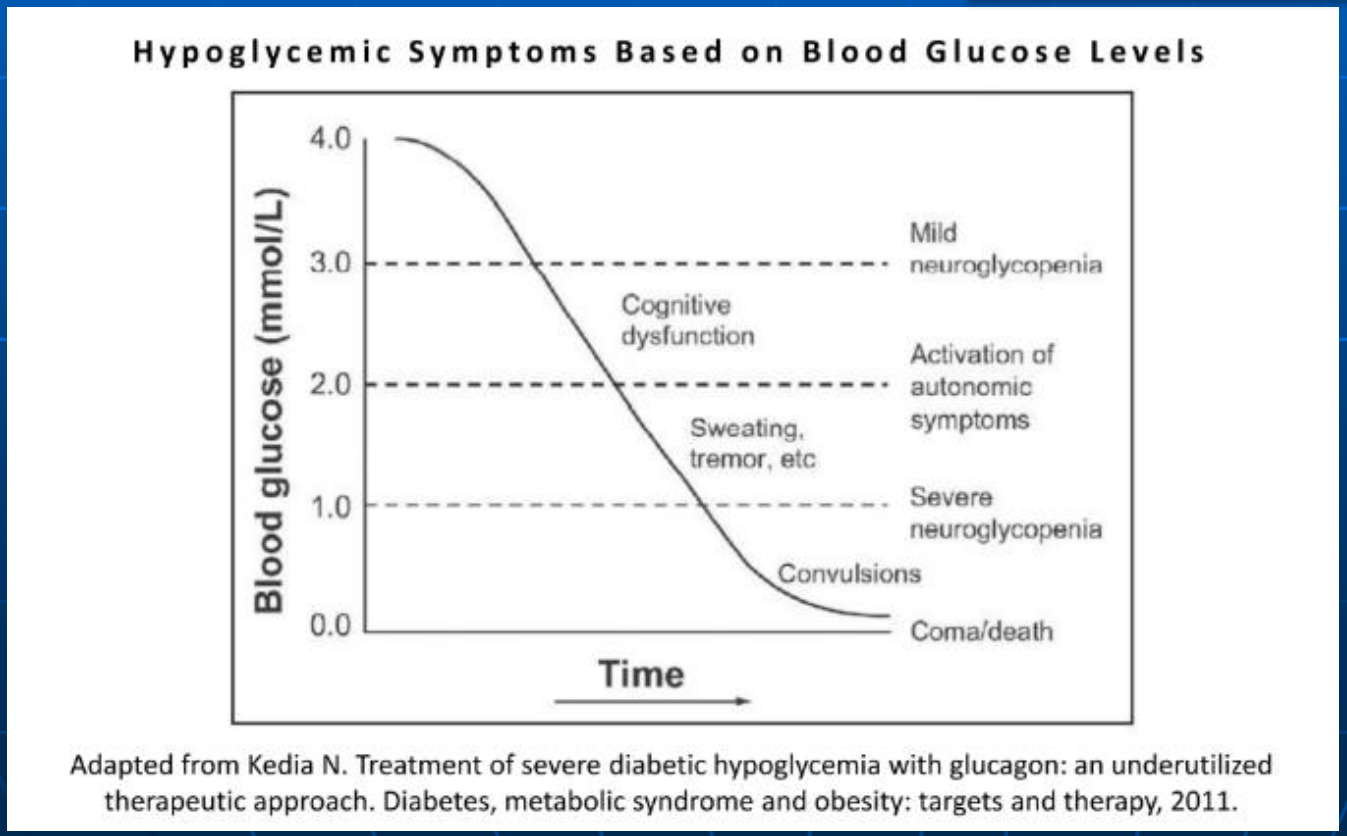
Clinical manifestations

Table 1: Symptoms of Hypoglycemia

AUTONOMIC	NEUROGLYCOPENIA
▪ Trembling ▪ Palpitations ▪ Sweating ▪ Anxiety ▪ Hunger ▪ Nausea ▪ Tingling	▪ Difficulty concentrating ▪ Confusion ▪ Weakness ▪ Drowsiness ▪ Vision changes ▪ Difficulty speaking ▪ Headache ▪ Dizziness

癥狀與血糖值都有相關性



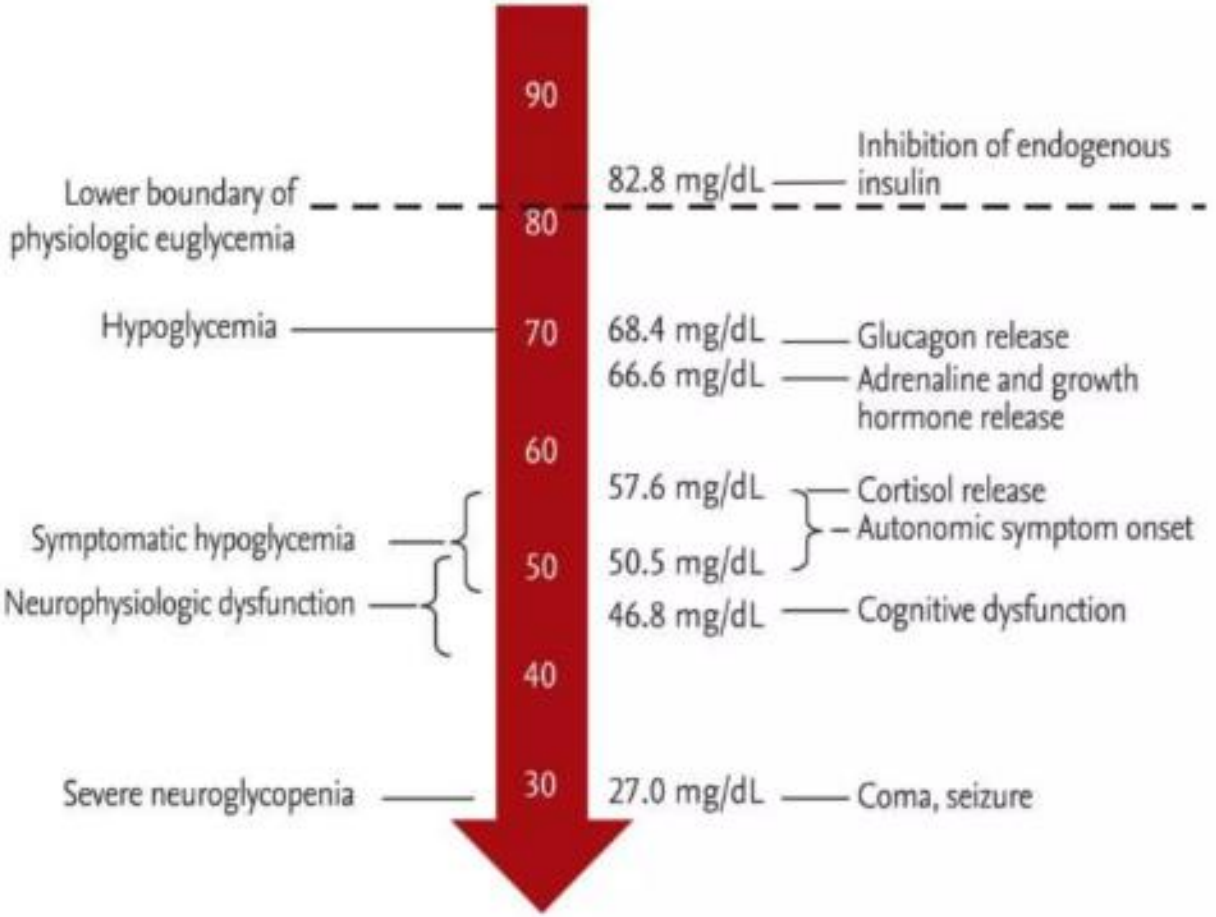


Adapted from Kedia N. Treatment of severe diabetic hypoglycemia with glucagon: an underutilized therapeutic approach. Diabetes, metabolic syndrome and obesity: targets and therapy, 2011.

血糖值越低癥狀越嚴重

CLINICAL FEATURES

Hypoglycemic Symptoms Based on Blood Glucose Levels



Severity

CLINICAL FEATURES

Table 2: Severity of Hypoglycemia

Mild	Autonomic symptoms are present. The individual is able to self-treat.
Moderate	Autonomic and neuroglycopenic symptoms are present. The individual is able to self-treat.
Severe	Individual requires assistance of another person. May become unconscious, plasma glucose is usually less than 2.8 mmol/L.

Not all of the above manifestations occur in every case of hypoglycemia. There is no consistent order to the appearance of the symptoms, if symptoms even occur. Specific manifestations may also vary by age, by severity of the hypoglycemia and the speed of the decline.

In both young and old patients, the brain may habituate to low glucose levels, with a reduction of noticeable symptoms despite neuroglycopenic impairment.

In **insulin-dependent diabetic patients** this phenomenon is termed **hypoglycemia unawareness** and is a significant clinical problem when improved glycemic control is attempted.

Diagnostic evidence

- 1. Blood sugar < 50 mg/dl
- 2. Hypoglycemic symptoms—
- autonomic symptoms
- neuro symptoms
- 3. Presence of precipitating factors.
- (Insulin injection, poor oral intake--)
- **4. Better after sugar supply by meal or IV**
- **glucose.**

Symptoms: 癥狀之表現 different in different age groups.

CLINICAL FEATURES

- In **young children**, vomiting can sometimes accompany morning hypoglycemia with ketosis.
- In **older children and adults**, moderately severe hypoglycemia can resemble mania, mental illness, drug intoxication, or drunkenness.
- In the **elderly**, hypoglycemia can produce focal stroke-like effects or a hard-to-define malaise.
- In **newborns**, hypoglycemia can produce irritability, jitters, myoclonic jerks, cyanosis, respiratory distress, apneic episodes, sweating, hypothermia, somnolence, hypotonia, refusal to feed, and seizures. Hypoglycemia can resemble asphyxia, hypocalcemia, sepsis, or heart failure.

病人為什麼要住院?
High risk of recurrent/prolonged hypoglycemia

Patients without other indication for admission but at high risk of prolonged/recurrent hypoglycemia should be considered for admission, examples :

- Patients on glibenclamide who cannot tolerate orally (because of the long half life, IV dextrose may be needed for days)
- Frail or elderly patients > 60 years old , especially if poor oral intake or poor social support.
- Patients with significant renal or liver impairment
- Patients who presented with recurrent episodes of hypoglycemia within the last 2 weeks
- Patients who are unable to self-care and unable to be discharged to an able caregiver
- Patient with previous history of severe hypoglycemia.

怕Prolonged hypoglycemia
Profound hypoglycemia
治療-→normal blood sugar

Sarawak Handbook of Medical Emergencies

Aims

AIM OF TREATMENTS

The **aims of treatment** are to:

a) Detect and treat a low blood glucose level promptly.

b) Eliminate the risk of injury to oneself and to relieve symptoms quickly.

c) Avoid overcorrection of hypoglycaemia especially in repeated cases as this will lead to poor glycaemic control and weight gain.

Treatment choice

A. Oral carbohydrate replacement
B. IV glucose/dextrose
C. Glucagon
D. Octreotide
E. Diazoxide

1.Treat of Hypoglycemic Episodes

Prevention is better than cure, and correction should be as quick as possible.

A. Fully conscious patients:

- In **mild to moderate hypoglycaemia** where the individual is able to self-treat, he/she should ingest 15 grams of simple carbohydrate (e.g **1 table spoon of honey**, **¾ cup of juice**, **3 tea spoon of table sugar**)

- Repeat blood glucose after 15 minutes. If the level at 15 minutes is still <4.0 mmol/L, another 15 grams of carbohydrate should be taken.

- In **severe hypoglycaemia** where the individual is still conscious, he/she should ingest 20 grams of carbohydrate and the above steps are repeated.

1.Treat of Hypoglycemic Episodes

B. When mental function is impaired:

Medical emergency : Set IV line, turn patient to the left lateral position.

- In severe hypoglycaemia and unconscious individual, he/she should be given 20–50 mL of IV 50% dextrose 25-50 ml over 1-3 minutes followed by saline flush. Outside the hospital setting, a tablespoon of honey should be administered into the oral cavity.

- Once hypoglycaemia has been reversed, the patient should have the usual meal or snack that is due at that time of the day to prevent repeated hypoglycaemia.

- When hypoglycemia is due to an overdose of long acting insulin or OADs, 10% dextrose drip should be continued for 24-48 hours.

- Patients receiving anti-diabetic agents that may cause hypoglycaemia should be counselled about strategies for prevention, recognition and treatment of hypoglycaemia. Individuals may need to have their insulin regimen adjusted appropriately to lower their risk.

- **Glucagon, 1 mg IM or deep SC** can be given to treat severe hypoglycemia when IV access is difficult. This option can also be taught to relatives of patients on insulin. As soon as patient regain consciousness after glucagon, they are advised to eat/drink (**followed procedure in (A)**) as the hyperglycemic action of glucagon lasts only for 10-15 min.

- Patient who remain unconscious after prolonged hypoglycemia may need to be given treatment for cerebral edema with IV dexamethasone 4 mg 6 hourly or IV mannitol, or consider other causes of coma (e.g. stroke, drug overdose)

先治療再查原因

2. Investigate and treat the underlying cause to prevent recurrence:

A. Adjustment of drug therapy, diet and physical activity

If hypoglycemia recurs at a particular time of day, change the distribution and timing of insulin injections.

If hypoglycemia is severe, prolonged, or unpredictable, reduce total dose.

Increase carbohydrates intake prior to increasing or prolonging activity/exercise.

Avoid long acting sulfonylureas like glinbeclimide in elderly patient or patient with renal impairment.

B. Educate patient on hypoglycemia recognition and management

C. For patients not known to have DM, please refer to endocrinologist for formal workup of hypoglycemia.

Octreotide:
antidote for sulfonylurea induced hypoglycemia

OCTREOTIDE

- Somatostatin analogue
- An antidote for sulfonylurea-induced hypoglycemia. Octreotide is a safe and effective treatment for refractory sulfonylurea-induced hypoglycemia, reducing additional hypoglycemic episodes.
- **Provides more potent inhibition of growth hormone, glucagon, and insulin as compared to endogenous somatostatin**
- May reduce recurrent hypoglycemia as with dextrose-alone therapy
- Should be used with IV dextrose/oral carbohydrates
- It is reserved for patients that experience a recurrent episode of hypoglycemia after standard dextrose therapy to prevent additional recurrences
- **Dose:** (ideal dose not well established)

  SQ: 50-100 mcg, repeat every 6 hours PRN

  IV: up to 125 mcg/hour has been used

Octreotide -2

OCTREOTIDE

- **Warnings/precautions:**
  I. Cholelithiasis – may inhibit gallbladder contractility
  II. Glucose regulation
  III. Hypothyroidism – may suppress TSH secretion
  IV. Pancreatitis – may change absorption of fats
- **Adverse effects:** bradycardia, dizziness, hyperglycemia, diarrhea, constipation

Diazoxide:
antidote for hypoglycemia due to hyperinsulionemia

DIAZOXIDE

- Antidote for hypoglycemia due to hyperinsulinemia; vasodilator
- Opens ATP-dependent K+ channels on pancreatic beta cells → hyperpolarization of the beta cell → inhibition of insulin release
- Binds to a different site on the potassium channel than the sulfonylureas
- Dose: 3-8 mg/kg/day PO in divided doses Q8H
  Starting dose 3 mg/kg/day PO divided in 2-3 doses
- **Contraindications:** hypersensitivity to diazoxide or to other thiazides
- **Warnings/precautions:**
  I. Heart failure – antidiuretic actions, may ↑ fluid retention
  II. Gout – may cause hyperuricemia
  III. Renal dysfunction
- **Adverse effects:** hypotension, hyperglycemia

Prevention of hypoglycemic episode

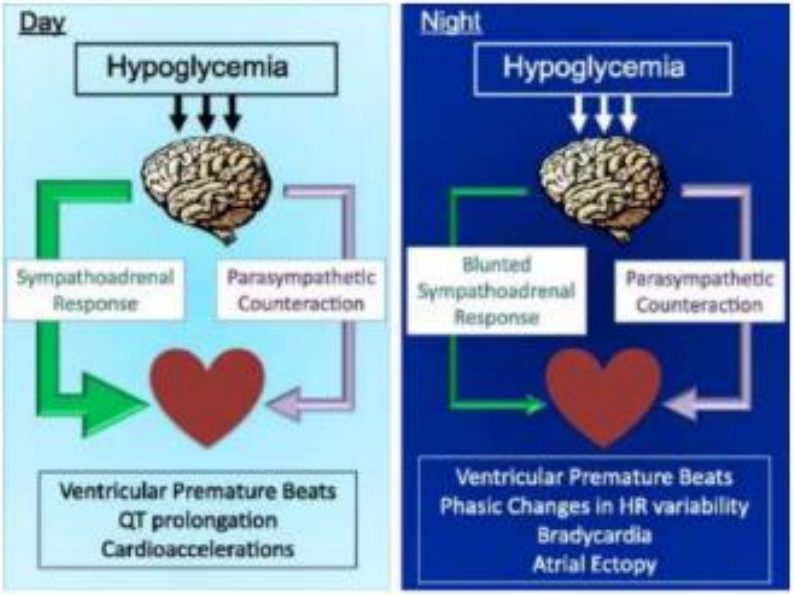
HOW TO PREVENT ?

To prevent future episodes of hypoglycemia

Note: Do not give correction insulin until next meal

Note: Basal insulin should never be held in patients with type 1 diabetes, but dose may require reduction

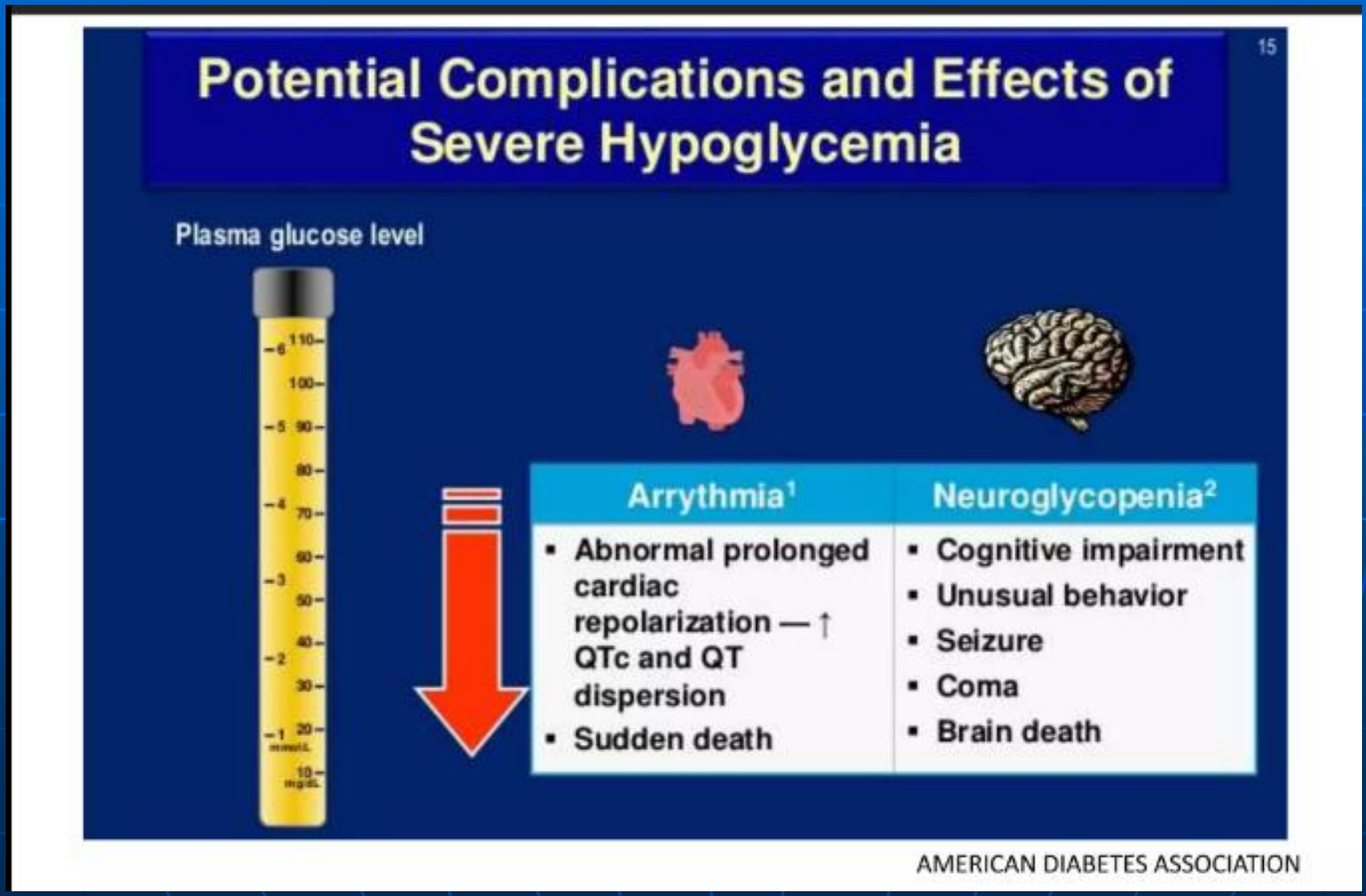
- Identify and correct the cause of the initial hypoglycemic episode
- Adjust nutritional insulin dose to match caloric (carbohydrate) intake or below goal pre-meal blood glucose.
- Document meals and snacks and ensure accurate and timely blood glucose monitoring
- Evaluate for early signs/symptoms of hypoglycemia.
- Pay attention to the blood glucose trends: contact provider if unusual or rapid downward blood glucose trend.
- Patients at high risk for severe hypoglycaemia should be informed of their risk and counselled, along with their family members and friends. Patients at risk of hypoglycaemia are discouraged from driving, riding, cycling or operating heavy machineries, as these activities may endanger oneself and the public.



Recommendations: Hypoglycaemia

1. Patients with frequent hypoglycaemia are prohibited from driving, riding, cycling or operating heavy machinery. *[Grade C]*
2. Patients must be educated on symptoms, risks and treatment of hypoglycaemia. *[Grade C]*
3. Hypoglycaemia unawareness should trigger re-evaluation of the treatment regimen. *[Grade C]*
4. In patients with hypoglycaemia unawareness and those with concomitant cardiovascular disease,

Complications of hypoglycemia



SITUATION

Hypoglycaemia – blood glucose level <4mmol/L

- A potentially dangerous side effect of insulin therapy and sulphonylureas
- Prompt treatment is required

BACKGROUND

Common causes of hypoglycaemia

- Inadequate food intake, fasting, delayed or missed meals
- Too much insulin or sulphonylurea
- Insulin administration/drug administration at an inappropriate time
- Problems with insulin injection technique/injection site causing variable insulin absorption
- Increased physical activity
- Alcohol

At risk groups

- Strict glycaemic control, impaired hypoglycaemic awareness, cognitive impairment, extremes of age, breast feeding mother with diabetes

Conditions that increase risk of hypoglycaemia

- Malabsorption, gastroparesis
- Abrupt discontinuation of corticosteroids, hypoadrenalism, renal or hepatic impairment, pancreatectomy

脂肪肥大Lipohypertrophy

ASSESSMENT

Assess recent pattern of blood glucose levels i.e. last 48 hours.

- Establish when and what the patient last ate
- Check insulin/ diabetes medication is being prescribed and administered at correct dose, time, and in relation to food intake
- Check for signs of lipohypertrophy (lumpy areas at injection sites) which may affect insulin absorption
- Check credibility of blood glucose monitoring e.g. handwashing before testing

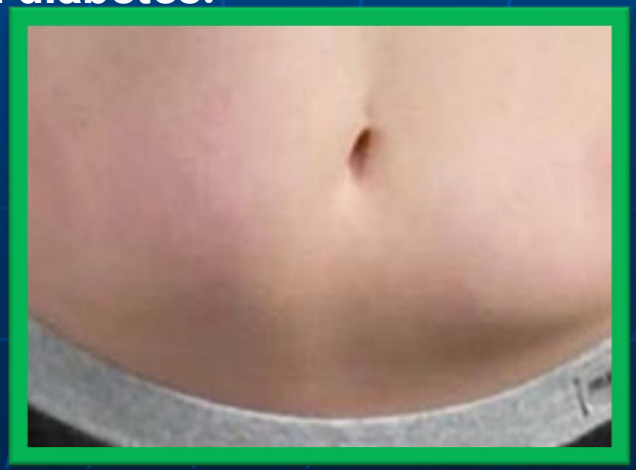
RECOMMENDATION

Treat hypoglycaemia as per protocol. Observe patient until recovery complete and provide information on hypoglycaemia management. Consult diabetes team for advice if necessary.

- Establish the cause of hypoglycaemia and take action to prevent recurrence. Inform patient if medication dose is changed
- **Do not omit insulin in type 1 diabetes** - treat hypoglycaemia and administer insulin as usual after dose review
- Blood glucose is likely to be high following hypoglycaemia; additional correction doses should not be given
- If receiving IV insulin treatment, check blood glucose every 15 minutes until above 4.0 mmol/L, then re-start IV insulin after review of infusion rates and requirement for IV insulin

Lipohypertrophy is a lump of fatty tissue under your skin caused by repeated injections in the same place. It's common in people with diabetes. Lipohypertrophy can affect your body's ability to absorb insulin and cause serious complications.

脂肪肥大的特徵是在身體注射部位周圍形成堅硬而緻密的腫塊。腫塊是反覆或過於頻繁使用胰島素注射部位時在皮下形成的脂肪組織堆積。儘管這些腫塊的大小和形狀可能會有所不同，但這種情況可能發生在任何通過注射或泵輸液管服用胰島素的人身上。



Algorithm for the Treatment and Management of Hypoglycaemia in Adults with Diabetes Mellitus in Hospital

Hypoglycaemia is a serious condition and should be treated as an emergency regardless of level of consciousness. Hypoglycaemia is defined as blood glucose of less than 4mmol/L (if not less than 4mmol/L but symptomatic give a small carbohydrate snack for symptom relief).

For further information see the full guideline "The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus" at **www.diabetes.nhs.uk**

Mild

Patient conscious, orientated and able to swallow

Give 15-20 g of quick acting carbohydrate, such as
5-7 Dextrosol® tablets or 4-5 Glucotabs®
or
90-120mls original Lucozade®,
or
150-200mls pure fruit juice**

Test blood glucose level after 15 minutes and if still less than 4 mmol/L repeat up to 3 times. If still hypoglycaemic, call doctor and consider IV 10% glucose at 100 ml/hr or 1mg Glucagon IM*.**

Moderate

Patient conscious and able to swallow, but confused, disorientated or aggressive

If capable and cooperative, treat as for mild hypoglycaemia

If not capable and cooperative but can swallow give 1.5-2 tubes of GlucoGel® (squeezed into mouth between teeth and gums). **If ineffective, use 1mg Glucagon IM*.**

Test blood glucose level after 10-15 minutes and if still less than 4 mmol/L repeat above up to 3 times. If still hypoglycaemic, call doctor and consider IV 10% glucose at 100 ml/hr.**

Severe

Patient unconscious/fitting or very aggressive or nil by mouth (NBM)

Check ABC, stop IV insulin, contact doctor urgently

Give IV glucose over 10 minutes as

75 ml 20% glucose or

150ml 10% glucose or

30ml 50% glucose (risk of extravasation injury, only use if 10%, 20% not available)

or 1mg Glucagon IM *

Recheck glucose after 10 minutes and if still less than 4mmol/L, repeat treatment.

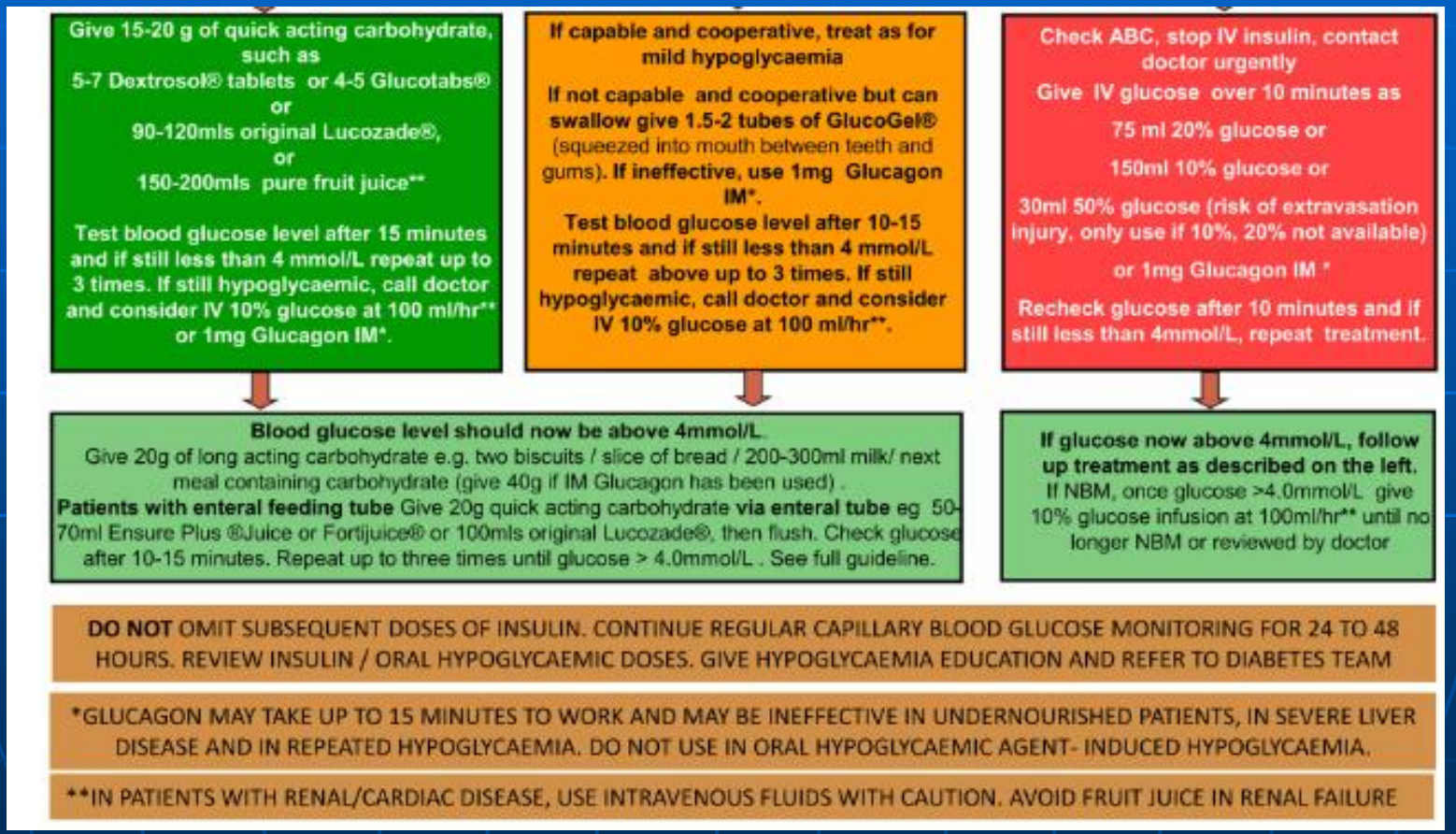
Blood glucose level should now be above 4mmol/L

Give 20g of long acting carbohydrate e.g. two biscuits / slice of bread / 200-300ml milk/ next meal containing carbohydrate (give 40g if IM Glucagon has been used) .

Patients with enteral feeding tube Give 20g quick acting carbohydrate **via enteral tube** eg 50-70ml Ensure Plus ®Juice or Fortijuice® or 100mls original Lucozade®, then flush. Check glucose after 10-15 minutes. Repeat up to three times until glucose > 4.0mmol/L . See full guideline.

If glucose now above 4mmol/L, follow up treatment as described on the left.

If NBM, once glucose >4.0mmol/L give 10% glucose infusion at 100ml/hr** until no longer NBM or reviewed by doctor

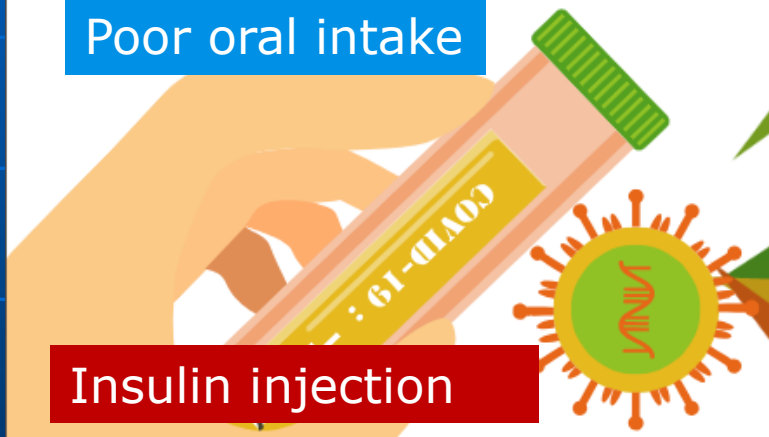

Give 15-20 g of quick acting carbohydrate, such as
5-7 Dextrosol® tablets or 4-5 Glucotabs®
or
90-120mls original Lucozade®,
or
150-200mls pure fruit juice**
Test blood glucose level after 15 minutes and if still less than 4 mmol/L repeat up to 3 times. If still hypoglycaemic, call doctor and consider IV 10% glucose at 100 ml/hr** or 1mg Glucagon IM*.
If capable and cooperative, treat as for mild hypoglycaemia
If not capable and cooperative but can swallow give 1.5-2 tubes of GlucoGel® (squeezed into mouth between teeth and gums). If ineffective, use 1mg Glucagon IM*.
Test blood glucose level after 10-15 minutes and if still less than 4 mmol/L repeat above up to 3 times. If still hypoglycaemic, call doctor and consider IV 10% glucose at 100 ml/hr**.
Check ABC, stop IV insulin, contact doctor urgently
Give IV glucose over 10 minutes as
75 ml 20% glucose or
150ml 10% glucose or
30ml 50% glucose (risk of extravasation injury, only use if 10%, 20% not available)
or 1mg Glucagon IM *
Recheck glucose after 10 minutes and if still less than 4mmol/L, repeat treatment.
Blood glucose level should now be above 4mmol/L.
Give 20g of long acting carbohydrate e.g. two biscuits / slice of bread / 200-300ml milk/ next meal containing carbohydrate (give 40g if IM Glucagon has been used) .
Patients with enteral feeding tube Give 20g quick acting carbohydrate via enteral tube eg 50-70ml Ensure Plus ®Juice or Fortijuice® or 100mls original Lucozade®, then flush. Check glucose after 10-15 minutes. Repeat up to three times until glucose > 4.0mmol/L . See full guideline.
If glucose now above 4mmol/L, follow up treatment as described on the left.
If NBM, once glucose >4.0mmol/L give 10% glucose infusion at 100ml/hr** until no longer NBM or reviewed by doctor
DO NOT OMIT SUBSEQUENT DOSES OF INSULIN. CONTINUE REGULAR CAPILLARY BLOOD GLUCOSE MONITORING FOR 24 TO 48 HOURS. REVIEW INSULIN / ORAL HYPOGLYCAEMIC DOSES. GIVE HYPOGLYCAEMIA EDUCATION AND REFER TO DIABETES TEAM
*GLUCAGON MAY TAKE UP TO 15 MINUTES TO WORK AND MAY BE INEFFECTIVE IN UNDERNOURISHED PATIENTS, IN SEVERE LIVER DISEASE AND IN REPEATED HYPOGLYCAEMIA. DO NOT USE IN ORAL HYPOGLYCAEMIC AGENT- INDUCED HYPOGLYCAEMIA.
**IN PATIENTS WITH RENAL/CARDIAC DISEASE, USE INTRAVENOUS FLUIDS WITH CAUTION. AVOID FRUIT JUICE IN RENAL FAILURE

Hypoglycemia in Diabetes

COVID-19

RISK FACTOR

Poor oral intake



Insulin injection

insulin (or insulin secretagogue) doses are excessive, ill-timed, or of the wrong type

influx of exogenous glucose is reduced

insulin-independent glucose utilization is increased

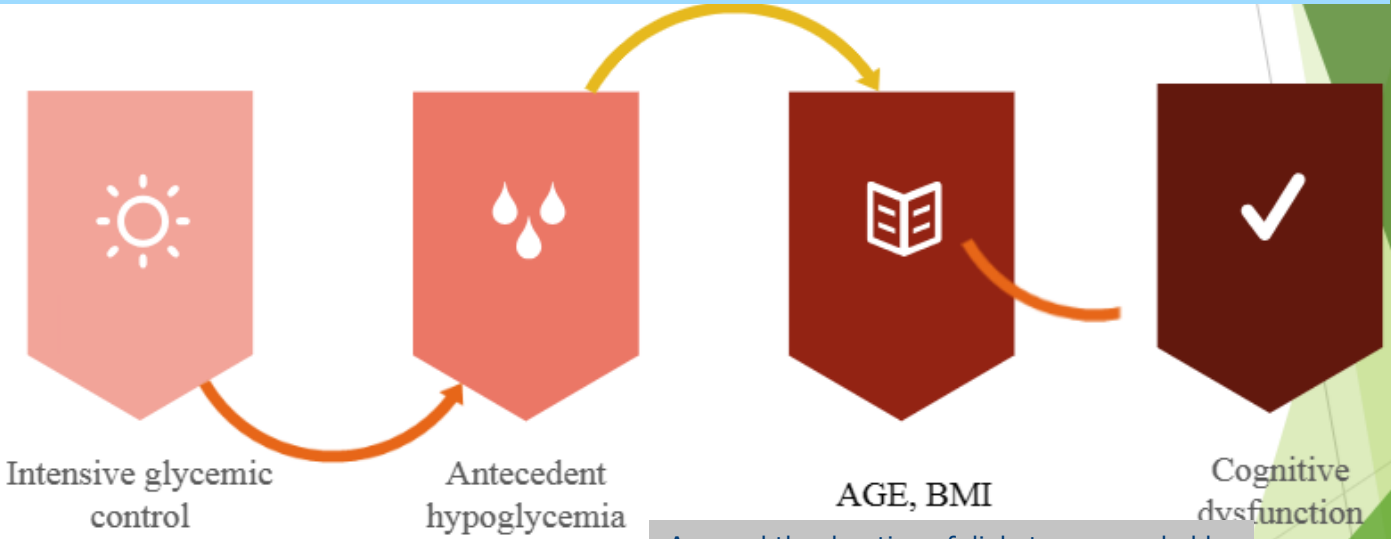
endogenous glucose production is reduced

Renal impairment

Factors related to hypoglycemia in DM

HYPOGLICEMIA IN DM

Quilliam et al. [16] suggested that a previous incidence of hypoglycemia was an independent predictor of SH in T2DM patients. In addition to traditional risk factors associated with hypoglycemia, they evaluated the increased rate of inpatient admission for SH after outpatient medical (odds ratio [OR], 7.88;or emergency department visits (OR, 9.48;) for hypoglycemia in the previous 6 months



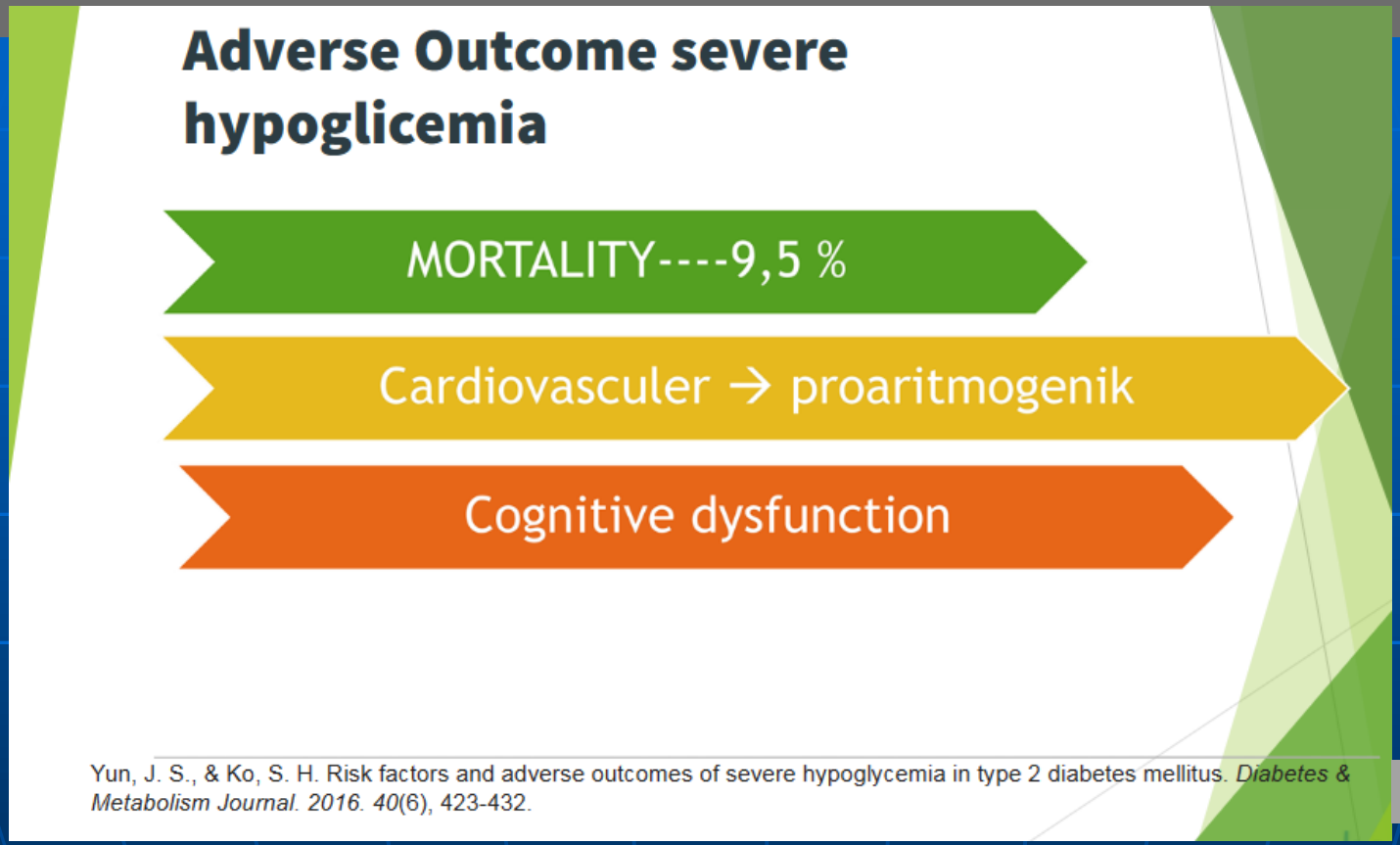
Age and the duration of diabetes are probably significant predictors for development of SH in those with T2DM

Yun, J. S., & Ko, S. H. Risk factors and adverse outcomes of severe hypoglycemia in type 2 diabetes mellitus. *Diabetes & Metabolism Journal. 2016. 40*(6), 423-432.

selecting a safer class of drugs for hypoglycemia

L1093,L1094)

Outcome of severe hypoglycemia



Yun, J. S., & Ko, S. H. Risk factors and adverse outcomes of severe hypoglycemia in type 2 diabetes mellitus. *Diabetes & Metabolism Journal. 2016. 40*(6), 423-432.

L1093,L1094

In the ADVANCE study, SH was associated with an increased risk of major macrovascular events (HR, 2.88; 95% CI, 1.19 to 4.19) [27]. In a systematic review and meta-analysis of cohort studies that included 903,510 patients with T2DM, SH was associated with a 2-fold increased risk of CVD [50]. Recent retrospective Japanese reports showed that SH was strongly associated with the risk of CVD (HR, 3.39)

Ten recommendations by the Amer. Endocrine Society in 2023.

- L1064. Anthony L. McCall, David C. Lieb,Roma Gianchandani,et al : Management of Individuals With Diabetes at High Risk for Hypoglycemia: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, 2023, 108, 529–562 .
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9
- 10.

問題 1.對於每天多次注射的 1 型糖尿病患者，是否應該使用連續血糖監測與自我血糖監測？

- Question 1. Should continuous glucose monitoring vs selfmonitoring of blood glucose be used for people with type 1 diabetes receiving multiple daily injections? **Recommendation 1**. We recommend continuous glucose monitoring (CGM) rather than **self-monitoring of blood glucose (SMBG)** by fingerstick for patients with type 1 diabetes (T1D) receiving multiple daily injections (MDIs). (1⊕⊕OO)
- Remarks • Comprehensive patient education on how to use and troubleshoot CGM devices and interpret these data is critically important for maximum benefit and successful outcomes. • SMBG continues to be necessary to validate or confirm CGM values; for example, when symptoms do not match sensor glucose values and during the sensor warm-up period. Therefore, patients using CGM must continue to have access to SMBG

建議的理由

- 儘管證據品質低，但該小組認為，**醫源性低血糖**是糖尿病血糖管理的限制因素，並且是糖尿病患者及其家庭成員的主要關注因素（44,45）。 建議任何患有 T1D 的人使用 CGM，對於患有 IAH、害怕低血糖的人以及有功能性低血糖意識的幼兒（他們的父母通常由於害怕夜間低血糖而睡不好）更強烈地使用 CGM。避免低血糖是當務之急，因為它會增加反覆和更嚴重的低血糖（意識喪失或癲癇發作）的風險，並且與血糖控制的不穩定性增加有關;QOL差;糖尿病困擾;駕駛或操作危險機械時可能造成嚴重傷害;對大腦和心臟的損害;而且，很少是死亡。
- **顯示葡萄糖水平變化方向和速率的趨勢箭頭使CGM用戶能夠預測未來30至60分鐘的葡萄糖水準，並做出更明智的管理決策**（46,47）。 已發表的研究未捕獲此資訊。早期版本的 CGM 需要多次每日校準，並且管理決策不能基於從 CGM 獲得的葡萄糖值（需要確認指尖 BG 測量）。與現已過時的早期 CGM 系統相比，**它們具有更高的精度、更長的使用時間以及無需校準或需要更少校準的頻率，因此較新的 CGM 系統的可接受性有所提高**。這反映在所有年齡段，尤其是幼兒（48,49）中CGM的使用增加。

問題 2.對於1型糖尿病患者，是否應該使用實時連續血糖監測和演算法驅動的胰島素泵，而不是每天多次注射，每天三次或更多次自我監測血糖？

2.對於患有1型糖尿病（T1D）的成人和兒童，我們建議使用實時連續血糖監測（CGM）和演算法驅動的胰島素泵（ADIP），而不是每日多次注射（MDI），並每天進行3次或更多次自我監測血糖（SMBG）。（2⊕⊕OO）

- 2. Question 2. Should real-time continuous glucose monitoring and algorithm-driven insulin pumps vs multiple daily injections with self-monitoring of blood glucose three or more times daily be used for people with type 1 diabetes?
- Recommendation 2 We suggest using **real-time continuous glucose monitoring (CGM) and algorithm-driven insulin pumps (ADIPs) rather than multiple daily injections (MDIs) with self-monitoring of blood glucose (SMBG) three or more times daily for adults and children with type 1 diabetes (T1D). (2⊕⊕OO)**
- **Remark. Fingerstick blood glucose (BG)** monitoring may still be necessary to validate or confirm CGM values; therefore, with respect to use and insurance coverage, there will be times when SMBG must be used.

- 建議的理由

- 由於缺乏證據來證明使用即時CGM和ADI與MDI和
- SMBG的相對利弊，小組成員依靠用於支持建議1中使用
- CGM與SMBG的建議的證據來證明其建議的合理性。此
- 外，小組成員還受到患者對使用即時 CGM 和 ADIP 管理
- 糖尿病的好處所表達的意見的影響。

問題 3.對於在門診服用胰島素和/或磺脲類藥物且低血糖風險高的 2 型糖尿病患者，是否應使用專業或個人實時連續血糖監測與不連續血糖監測？

- 3. Question 3. Should professional or personal real-time continous glucose monitoring vs no continous glucose monitoring be used for people with type 2 diabetes in the outpatient setting who take insulin and/or sulfonylureas and are at high risk for hypoglycemia?
- Recommendation 3 We suggest **real-time continous glucose monitoring (CGM) be used** rather than no continuous glucose monitoring (CGM) for outpatients with type 2 diabetes (T2D) who take insulin and/or sulfonylureas (SUs) and are at risk for hypoglycemia. (2⊕OOO
- Remarks • Professional CGM is a diagnostic tool used for the shortterm investigation of an individual's glycemic profile to determine glycemic patterns and to assist with therapeutic management. • Personal CGM is a tool for patients to use in real time at home to assist the patient and their health care providers (HCPs) in making both short- and long-term adjustments in their therapeutic management

問題 4.對於低血糖高危人群，是否應在住院期間開始連續血糖監測，而不是不使用連續血糖監測？

- 4. Question 4. Should initiation of continuous glucose monitoring in the inpatient setting vs not using continuous glucose monitoring be used for select people at high risk for hypoglycemia?
- Recommendation 4 We suggest **initiation of continous glucose monitoring (CGM) in the inpatient setting for select inpatients at high risk for hypoglycemia.** (2⊕OOO) Remarks • This should be performed via a hybrid approach in which CGM use is combined with periodic point-of-care blood glucose (POC-BG) testing to validate the accuracy of CGM. • Inpatient CGM use is not currently approved by the US Food and Drug Administration (FDA) but currently has enforcement discretion. It has been used in hospitals recently with emergency use authorization during the COVID-19 pandemic

問題 5.低血糖高危人群已經在使用，是否應該在住院環境中繼續進行個人連續血糖監測或停止連續血糖監測？

- 5. Question 5. Should continuation of personal continuous glucose monitoring in the inpatient setting vs discontinuation of continuous glucose monitoring be used for people at high risk for hypoglycemia who are already using it?
- **Recommendation 5** We suggest **continuation of personal continuous glucose monitoring (CGM**) in the inpatient setting with or without algorithm-driven insulin pump (ADIP) therapy rather than discontinuation. (2⊕OOO)
- Remarks • This should be performed via a hybrid approach in which CGM use is combined with periodic point-of-care blood glucose (POC-BG) testing to validate the accuracy of CGM. • Inpatient CGM use is not currently approved by the US Food and Drug Administration (FDA) but currently has enforcement discretion. It has been used in hospitals recently with emergency use authorization during the COVID-19 pandemic

問題 6.對於有低血糖風險的住院患者，是否應該使用利用電子健康記錄數據與標準護理的住院患者進行血糖監測和管理計劃？

- 6. Question 6. Should inpatient glycemic surveillance and management programs leveraging electronic health record data vs standard care be used for hospitalized people at risk for hypoglycemia?
- Recommendation 6 We recommend that inpatient glycemic surveillance and management programs leveraging electronic health record (EHR) data be used for inpatients at risk for hypoglycemia. (1⊕OOO)
- Remarks • The panel defined leveraging EHR data as specific hospital staff using glycemic data collected within the EHR (from all admitted patients) to identify those at risk for and those having hypoglycemic and hyperglycemic episodes to develop mechanisms for managing and mitigating these adverse outcomes. Standard care is lack of such a program. • EHR data leveraged includes patterns of glycemia with proactive alerts for high and for low trends, so that hypoglycemia and severe hyperglycemia can be identified in a systematic fashion. Staff can then intervene on these trends (eg, adjusting insulin infusion rates) to avoid unwanted outcomes (repeat hypoglycemia, glycemic variability, etc).

問題 7.長效胰島素類似物與人胰島素相比，是否應該用於接受基礎胰島素治療且低血糖風險高的患者？

- 7, Question 7. Should long-acting insulin analogs vs human insulin be used for people on basal insulin therapy who are at high risk for hypoglycemia?
- Recommendation 7 We suggest long-acting insulin analogs be used rather than human neutral protamine Hagedorn (NPH) insulin for adult and pediatric outpatients on basal insulin therapy who are at high risk for hypoglycemia. (2⊕OOO)

- Remarks • Patients who are at high risk for hypoglycemia are defined as those with a history of severe hypoglycemia (requiring assistance to manage), impaired awareness of hypoglycemia (IAH), and/or medical conditions that predispose them to severe hypoglycemia including renal and hepatic dysfunction. • The panel placed high value on reducing severe hypoglycemia and found moderate-certainty evidence for severe hypoglycemia reduction as an outcome in those using long-acting analog insulins vs NPH insulin. However, the panel acknowledges that most studies of long-acting analog insulins do not assess for significant adverse effects (including cardiovascular outcomes) and that many studies were designed to demonstrate noninferiority of analog insulin compared with human NPH insulin.

問題 8.對於低血糖風險高的患者，是否應將速效類似物與常規（短效）人胰島素用於基礎推注治療？

- 8. Question 8. Should rapid-acting analogs vs regular (shortacting) human insulin be used for people on basal-bolus therapy who are at high risk for hypoglycemia?
- Recommendation 8 We suggest that rapid-acting insulin analogs be used rather than regular (short-acting) human insulins for adult and pediatric patients on basal-bolus insulin therapy who are at high risk for hypoglycemia. (2⊕OOO)
- Remarks • Patients who are at high risk for hypoglycemia are defined as those with a history of severe hypoglycemia (requiring assistance to manage), impaired awareness of hypoglycemia (IAH), and/or medical conditions that predispose them to severe hypoglycemia including renal and hepatic dysfunction. • The panel placed high value on reducing severe hypoglycemia and found moderate-certainty evidence for reduction of mild-to-moderate and severe hypoglycemia as an outcome in those using rapid-acting analog insulins vs regular (short-acting) insulin. However, the panel acknowledges that many studies were designed to demonstrate noninferiority of analog insulin compared with human regular (short-acting) insulin. Also, many of the data available for review demonstrating reductions in hypoglycemia were in adults with T1D; very few data were available regarding the pediatric population

問題 9.對於接受胰島素治療且低血糖風險高的患者，是否應採用結構化的患者教育計劃，包括隨訪與非結構化建議？

- 9. Question 9. Should a structured program of patient education with follow-up vs unstructured advice be used for people receiving insulin therapy who are at high risk for hypoglycemia? Recommendation 9 We recommend that **a structured program of patient education** over unstructured advice be used for adult and pediatric outpatients with type 1 diabetes (T1D) or type 2 diabetes (T2D) receiving insulin therapy. (1⊕⊕OO)
- **Remarks • Structured education on how to avoid repeated hypoglycemia is critical, and this education should be performed by experienced diabetes clinicians. Moreover, insurance coverage for education should be available for all insulin-using patients. • The recommendation is not intended to limit structured education only to those on insulin therapy; for example, patients using sulfonylureas (SUs) and meglitinides are also at risk for hypoglycemia, and the recommendation also applies to this patient population**

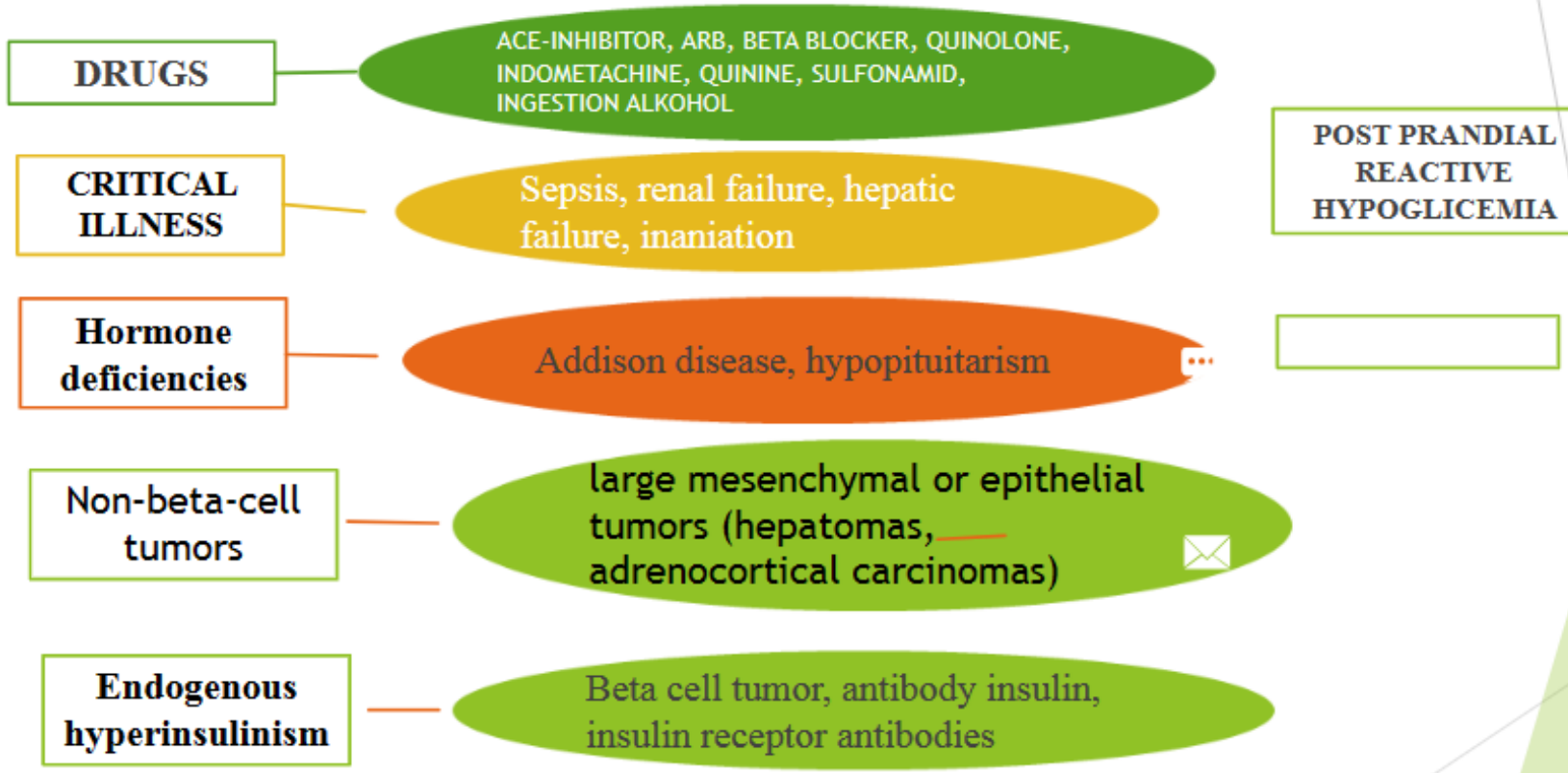
問題 10.對於重度低血糖患者，是否應該使用不需要復溶的胰高血糖素製劑與必須復溶的製劑？

Recommendation 10對於重度低血糖的門診患者，我們建議使用不需要復溶的胰高血糖素製劑(glucagon)，而不是必須復溶的胰高血糖素製劑（即，以粉末和稀釋劑形式提供）。（1⊕000）

- 10. Question 10. Should glucagon preparations that do not have to be reconstituted vs preparations that do have to be reconstituted be used for people with severe hypoglycemia?
- Recommendation 10 We recommend that glucagon preparations that do not have to be reconstituted over glucagon preparations that do have to be reconstituted (ie, available as a powder and diluent) be used for outpatients with severe hypoglycemia. **(1**⊕OOO)

II.

Hypoglycemia Without Diabetes



Desimone, M. E., & Weinstock, R. S. Non-diabetic hypoglycemia. In *Endotext [Internet]*. MDText. com, Inc. .2017.

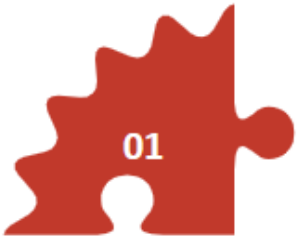
Whipple triad:
Hypoglycemia without DM

- If spontaneous hypoglycemia is suspected, the Whipple triad should be used to confirm hypoglycemia before pursuing further diagnostic workup.
- The Whipple criteria include the following:
- (1) low levels of plasma glucose,
- (2) signs or symptoms that would be expected with low levels of
- plasma glucose, and
- (3) improvement in those signs or symptoms when the level of plasma
- glucose increases.
- Spontaneous hypoglycemia can be caused by conditions that cause
- endogenous hyperinsulinism, including insulinoma, postbariatric
- hypoglycemia, and noninsulinoma pancreatogenous hypoglycemia.
- Spontaneous hypoglycemia can also be seen with critical illness, hepatic or renal
- dysfunction, hormonal deficiency, non-diabetes-related medications, and non-
- islet cell tumors

Gurunanthan Palani [1], et al (Minnesota Univ.)**Clinical Presentation and Diagnostic Approach to Hypoglycemia in Adults Without Diabetes Mellitus**
Endocr Pract. 2023 Apr;29(4):286-294.

Reactive hypoglycemia

REACTIVE HYPOGLICEMIA



Hipoglycemia 2-5 hours after food intake

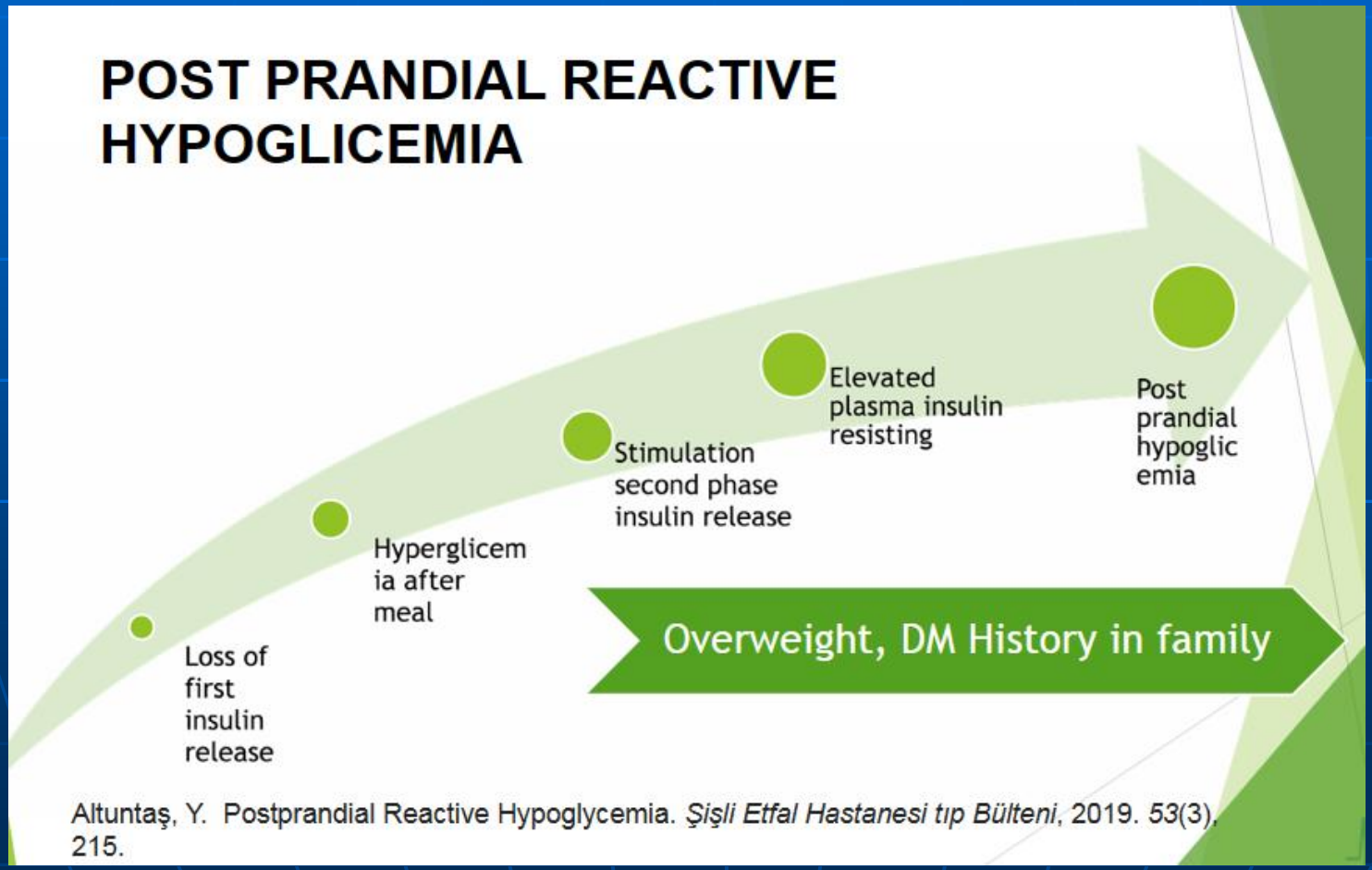
Prediabetic state

3 type :
- Early
- Idhiopatic
- Late

Terapi :
- Life style
- OAD (Metformin, AGI, DPP IV Inhibitor

Altuntaş, Y. Postprandial Reactive Hypoglycemia. *Şişli Etfal Hastanesi tıp Bülteni*, 2019. *53*(3), 215.

III. Postprandial reactive hypoglycemia.



Altuntaş, Y. Postprandial Reactive Hypoglycemia. *Şişli Etfal Hastanesi tıp Bülteni*, 2019. *53*(3), 215.

IV. Drugs related hypoglycemia

•Apart from the iatrogenic causes of hypoglycemia in a diabetic person [1],

•the most common etiologies are (Fig. 1):•

- other iatrogenic causes (sulfonamides, tramadol,
- topiramate, tyrosine kinase inhibitors etc.);
- surreptitious hypoglycemia (sulfonamides, glinides,
- insulin);

Hypoglycaemia related to tramadol, mechanism : poorly understood.

- An analysis of hypoglycaemia cases recorded in two pharmacovigilance databases between 1967 and 2018 supports the hypothesis of a class effect with opioids, which could be dose-dependent, with diabetic patients and women being more at risk [101]. In this study, tramadol was the opioid for which the most cases of hypoglycaemia were reported.
- An analysis of a US pharmacovigilance database over the same time period but using a different methodology also concluded that tramadol is the opioid most likely to be associated with hypoglycaemia and identifed a few cases related to tapentadol.
- To date, the pathophysiological mechanisms at the origin of opioid-induced hypoglycaemia remain poorly understood and debated. They may result from an increase in glucose central utilisation as a result of stimulation of mu-opioid receptors and some serotonergic receptors, which may account for the higher proportion of cases associated with tramadol and methadone (L1099)

臺灣的報告認定糖尿病病人使用 Tramadol 會比較容易發生低血糖

Shang-Yi Li [1], Hsin-Hung Chen [2 3 4 5], Cheng-Li Lin [6 7], Su-Yin Yeh [8], Chia-Hung Kao [9] **Association of Tramadol and Hypoglycemia in Diabetic Asians.** J Clin Med. 2018 Oct 24;7(11):380. (L1102)(L1103)

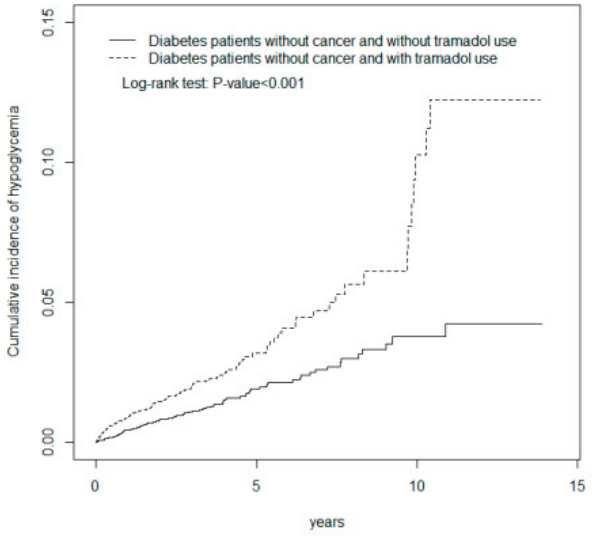


Figure 1. Cumulative incidence of hypoglycemia for patients with (dashed line) or without (solid line) tramadol use among diabetes patients without cancer.

Tramadol use increases hypoglycemic risk in diabetic patients. In this study, we should pay more attention to prevent hypoglycemia attack in those high risk diabetic patients who were older, with chronic kidney disease and prescribed medications such as insulin, sulfonylurea, metformin and loop diuretics in Asia.

V

INSULINOMA

Introduction

Most common functional Neuroendocrin Tumor (NET) → Hiperinsulin.

Solitary Benign Tumor

5% Malignant

ETIOLOGY Epidemiology

Not Clearly Understood

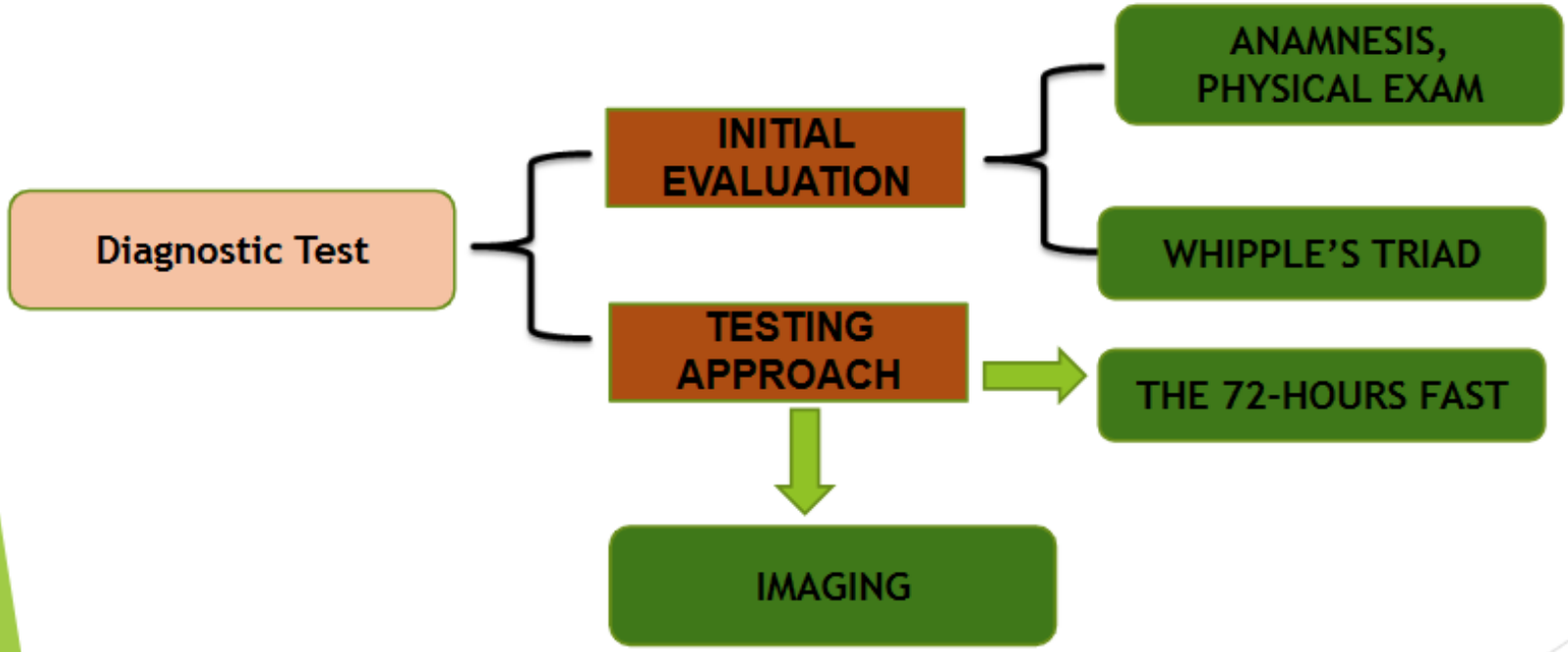
1-4/1.000.000 Per Tahun

Prognosis

10 Year Survival rate 88 % after surgical removal

Zhuo, F., & Anastasopoulou, C. Insulinoma. In *StatPearls [Internet]*. StatPearls Publishing. 2019

DIAGNOSTIC TEST



Zhuo, F., & Anastasopoulou, C. Insulinoma. In *StatPearls [Internet]*. StatPearls Publishing. 2019

Risky test.

THE 72 HOURS FASTING

- Gold Standard
- no food, non-essential medications should be discontinued.
- Simultaneous insulin, c-peptide and glucose samples are obtained at the beginning of the fast and every 4-6 hours.
- When the plasma glucose falls to <60 mg/dL, specimens should be taken every 1-2 hours under close supervision.
- The fast continues until plasma glucose less than 55 mg/dL is an alternative end point if Whipple's triad has been previously documented] and symptoms of neuroglucopenia develop.
- At this time insulin, glucose, c-peptide, oral insulin secretagogues, proinsulin are obtained and the fast is terminated

Desimone, M. E., & Weinstock, R. S. Non-diabetic hypoglycemia. In *Endotext [Internet]*. MDText. com, Inc. 2017

Distinguishing Causes of Symptomatic Hypoglycemia [glucose < 55 mg/dl After a Prolonged Fast

- Approximately 75% of patients with insulinomas are diagnosed after a 24 hour fast and 90-94% at 48 hours.

Insulin (μU/mL)	C-peptide (nmol/L)	Proinsulin (pmol/L)	Oral hypoglycemic medication	Interpretation
»3	<0.2	<5	No	Exogenous insulin
≥3	≥0.2	≥5	No	Endogenous insulin[a]
≥3	≥0.2	≥5	Yes	Oral hypoglycemic (drug-induced)

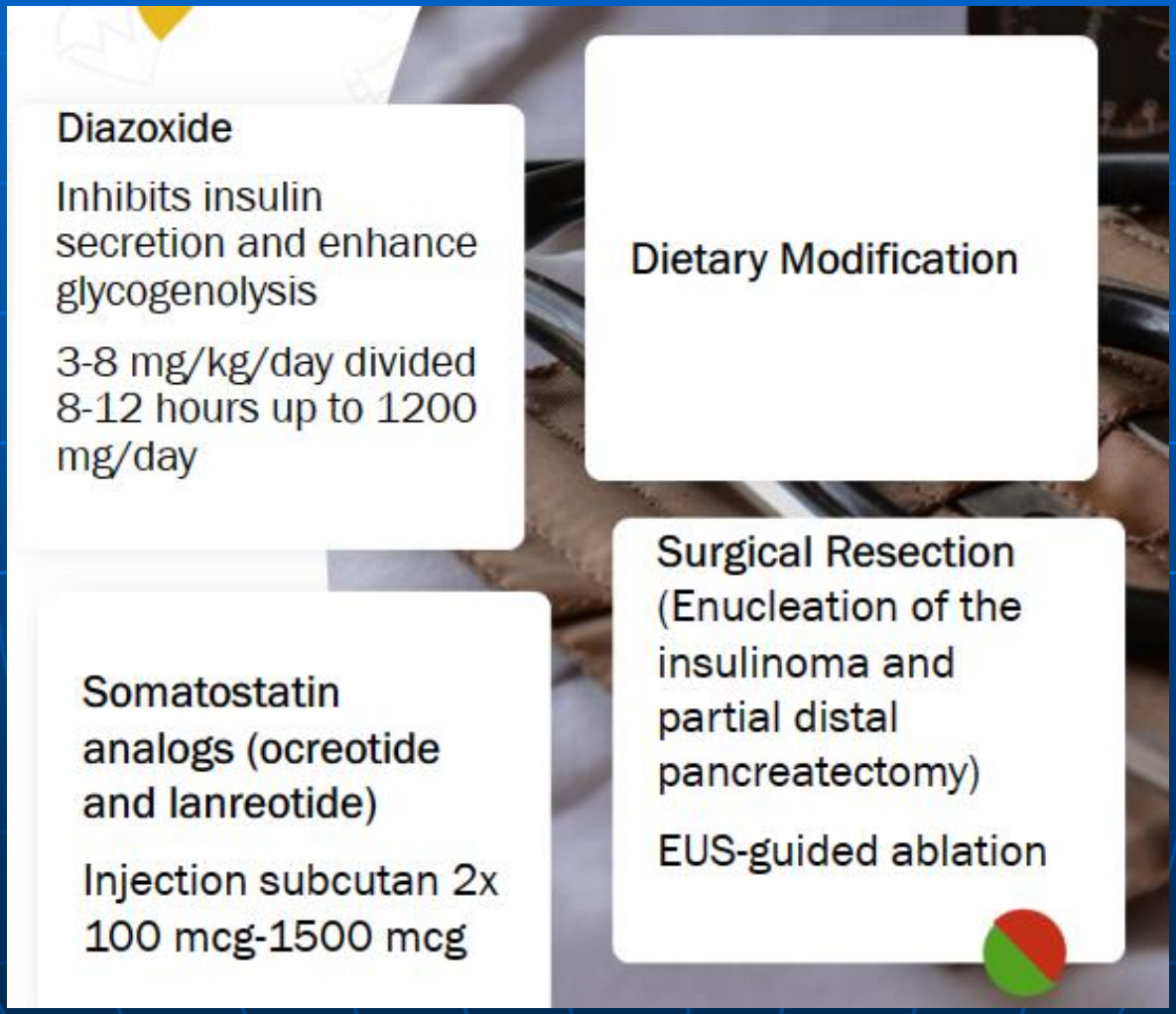
Desimone, M. E., & Weinstock, R. S. Non-diabetic hypoglycemia. In *Endotext [Internet]*. MDText.com, Inc. 2017

IMAGING

- computed tomography (CT), magnetic resonance imaging (MRI), GLP-1 receptor imaging.
- Imaging studies are successful in identifying insulinomas approximately 75% (CT scan), 85% (MRI), 66-97% (GLP-1)
- Negative imaging → Endoscopic ultrasonography (EUS) or selective arterial calcium stimulation test (SACST)
- EUS has sensitivy 70 - 95% identifying insulinomas
- SACST has sensitivity 93 % identifying insulinomas

Zhuo, F., Anastasopoulou, C. Insulinoma. In *StatPearls [Internet]*. StatPearls Publishing. 2019

Specific treatment of insulinoma



VI, Autoimmune hypoglycemia

Insulin autoimmune syndrome

- 胰島素自身免疫綜合征（IAS）是一種罕見的疾病，其特徵是由於存在高血清濃度的胰島素自身抗體（IAA）而自發性發作的高胰島素血症性低血糖。
- IAS也被命名為平田氏病(Hirata Disease)，這是在1970年由Yukimasa Hirata及其同事做出的原始描述.。
- [1]IAS是自身免疫性低血糖症的兩種類型之一，
- 另一種是B型: 胰島素抵抗(insulin resistance, which is due to antibodies against the insulin receptor.)，這是由於針對胰島素受體的抗體引起的。

Hirata Y, Ishizu H, Ouchi N. Insulin autoimmunity in a case of spontaneous hypoglycemia. *J Jpn Diabetes Soc*. 1970;**13**:312–320.

Daniele Cappellani [1] et al : **Insulin Autoimmune Syndrome (Hirata Disease): A Comprehensive Review Fifty Years After Its First Description.** Diabetes Syndr Obes. 2020 Apr 1:13:963-97 (L1105)

Table 1 Main Epidemiological Studies on Insulin Autoimmune Syndrome (IAS)

Authors	Year	Study Population	Estimated Incidence/Prevalence of IAS	Ethnicity of the Study Population	Reference
Takayama-Hasumi et al	1990	Patients admitted to 2094 Japanese hospitals for hypoglycemic episodes	Prevalence: 11.7% of a selected cohort (41 cases over 350 patients)	Japanese	[16]
Uchigata et al	1994	Reports of IAS published/presented in Japan from 1970 to 1992	Incidence: 9 cases per year (197 cases over 22 years)	Japanese	[22]
Uchigata et al	2000	Review of the published cases from 1970 to 1997	Incidence: 9 cases per year (244 cases over 27 years)	Japanese	[20]
			Incidence: 1 case per year (26 cases over 27 years)	Caucasian	
Uchigata et al	2009	Review of the published cases from 1970 to 2007	Incidence: 10.3 cases per year (380 cases over 37 years)	Worldwide	[14]
Woo et al	2015	Patients hospitalized for hyperinsulinemic hypoglycemia	Prevalence: 6% of a selected cohort (5 cases over 84 patients)	Korean	[18]
Wang et al	2015	Patients identified by a nationwide questionnaire survey on IAS	Incidence: 2.6 cases per year (73 cases over 28 years)	Chinese	[19]
Yamada et al	2019	Patients identified by a nationwide survey on endogenous hyperinsulinemic hypoglycemia	Prevalence: 4.9% of a selected cohort (22 cases over 447 patients). Estimated prevalence in the general population: 0.017 cases per 100.000 population	Japanese	[17]

1. Three hundred eighty cases of IAS were reported worldwide from 1970 to 2009. (Uchigata et al, 2009)

2. Yun-Lin Wang, Pei-Wei Yao[1], Xiao-Ting Zhang, et al (China) **Insulin Autoimmune Syndrome: 73 Cases of Clinical Analysis, Chinese Med J. (Eng)** 2015 Sep 5;128(17):2408-9

IAS的發病機制尚不完全清楚

- **IAS的發病機制尚不完全清楚**。最廣泛接受的理論是，IAS是由遺傳易感性與環境觸發因素相互作用的結果，從而導致產生具有致病作用的胰島素自身抗體。

The ages at onset varied widely, peaked at 60–69 years old for male but 30–39 years old for female. There was no remarkable sex difference across different age groups except the 30–39-year group, in which 85% were females.

Drugs taken before the onset of IAS in 73 patients with this disease

Drug	Associated disease	IAS patients (*n*)		
		Male	Female	Total
MTZ	Graves'	13	28	41
PTU	Graves'	4	2	6
MPG	Liver dysfunction	4	0	4
Captopril	Hypertension	1	1	2
Alpha lipoic acid	Diabetic peripheral neuropathy	1	3	4
Non-SH compounds		4	3	7
Total		27	37	64

MTZ, MPG and captopril are all sulfhydryl compounds.

Yun-Lin Wang, Pei-Wei Yao[1], Xiao-Ting Zhang, et al (China) **Insulin Autoimmune Syndrome: 73 Cases of Clinical Analysis, Chinese Med J. (Eng)** 2015 Sep 5;128(17):2408-9

Class	Medication	References	Strenght of the Association
Antithyroid drugs	Methimazole	[9,11,23,29,37–41]	High
	Carbimazole	[42–47]	Medium
Supplements	Alpha-lipoic acid	[33–35,48–52]	High
	Pyritinol	[53,54]	Low
	Glutathione	[21]	Low
	Methionine	[55]	Low
Antihypertensives	Captopril	[22,36]	Low
	Hydralazine	[56,57]	Low
	Procainamide	[56]	Low
	Diltiazem	[22]	Low
Antiplatelet drugs	Clopidogrel	[58,59]	Low
Oral antidiabetics	Tolbutamide	[22]	Low
	Gliclazide	[60]	Low
Anti-inflammatory drugs	Steroids	[22]	Low
	Loxoprofen-sodium	[61]	Low
	Diclofenac	[22]	Low
Muscle relaxants	Tolperisone hydrochloride	[22]	Low
Antibiotics	Penicillamine	[62,63]	Low
	Imipenem	[64]	Low
	Penicillin G	[65]	Low
	Isoniazid	[66]	Low
Proton pump inhibitors	Pantoprazole	[67]	Low
	Omeprazole	[68]	Low
Plasma proteins	Albumin	[69]	Low
Orphan drugs	Tiopronin (Mercaptopropionyl glycine)	[21,22]	Low

Notes: The strength of the association has been defined as low (less than 5 reports), medium (between 5 and 9 reports), or high (more than 10 reports).

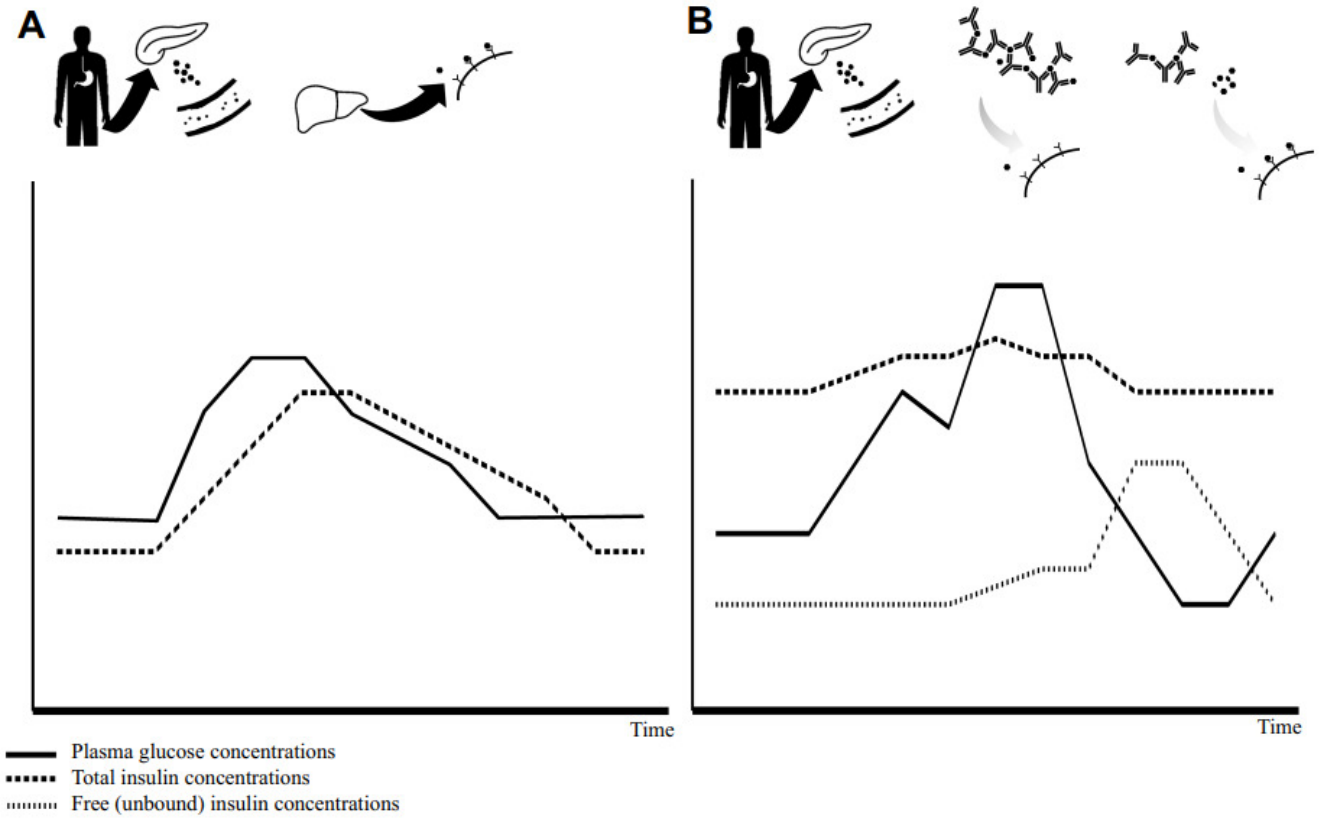
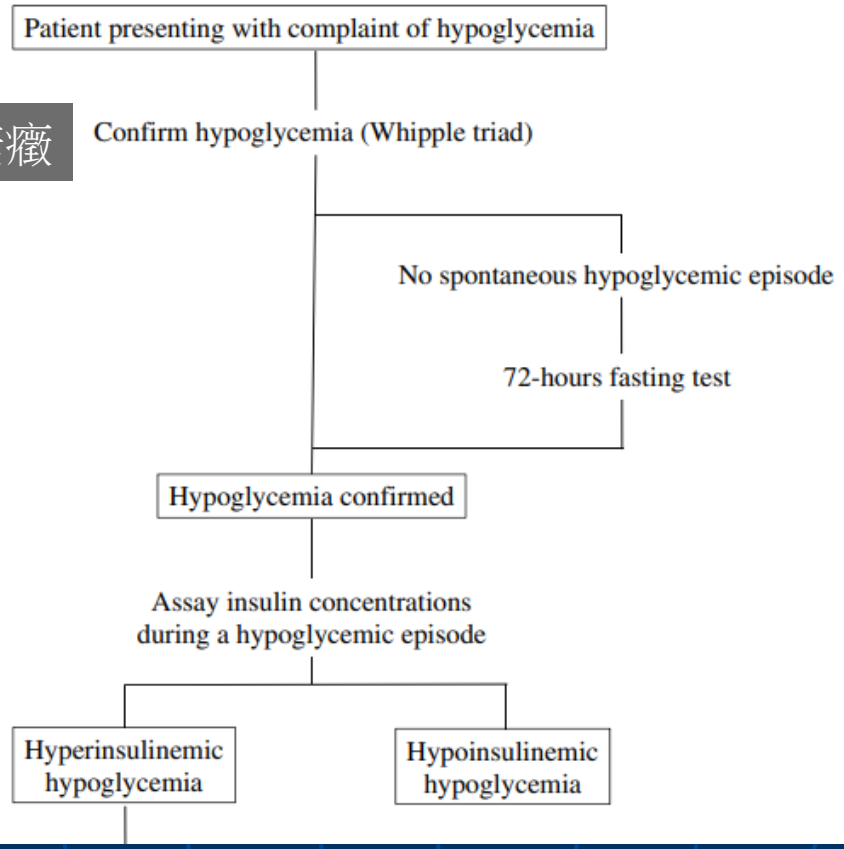


Figure 1 The insulin autoimmune syndrome pathogenesis.

Notes: Panel (**A**) schematic overview of the physiologic insulin secretion and action: following glucose intake, pancreatic beta-cells secrete insulin which enters into the bloodstream, getting to peripheral tissues when it exerts its physiological functions in order to maintain glucose homeostasis. Panel (**B**) schematic overview of the double-phase mechanism of the insulin autoimmune syndrome. Following glucose intake, pancreatic beta-cells secrete insulin which enters into the blood stream getting included in the insulin-IAA macro-complexes. In the early postprandial phase, inclusion intro macro-complexes prevents insulin to act on its receptors in peripheral tissues, thus inducing hyperglycemia (phase 1). Due to the relatively low affinity for insulin, IAA subsequently release insulin molecules irrespective of plasma glucose concentrations, thus inducing hypoglycemic episodes (phase 2). Below both panels is reported a schematic representation of glucose and insulin concentrations over time: the continuous line

圖（**A**）生理胰島素分泌和作用的示意圖概述：攝入葡萄糖后，胰腺β細胞分泌胰島素，胰島素進入血液，在發揮生理功能時到達外周組織，以維持葡萄糖穩態。圖（**B**）胰島素自身免疫綜合征雙相機制示意圖概述。攝入葡萄糖后，胰腺β細胞分泌胰島素，胰島素進入血液，包含在胰島素-IAA宏複合物中。在餐后早期，包涵體引入大複合物會阻止胰島素作用於外周組織中的受體，從而誘發高血糖症（第 1 階段）。由於對胰島素的親和力相對較低，IAA 隨後釋放胰島素分子，而與血漿葡萄糖濃度無關，從而誘導低血糖發作（第 2 階段）。在兩個面板下方報告了葡萄糖和胰島素濃度隨時間變化的示意圖：連續線表示血漿葡萄糖濃度，虛線表示總胰島素，尖線表示遊離未結合的胰島素。

第一步:確定有低血糖癥


Patient presenting with complaint of hypoglycemia
Confirm hypoglycemia (Whipple triad)
No spontaneous hypoglycemic episode
72-hours fasting test
Hypoglycemia confirmed
Assay insulin concentrations during a hypoglycemic episode
Hyperinsulinemic hypoglycemia
Hypoinsulinemic hypoglycemia

Whipple's triad.
: Insulinoma + others

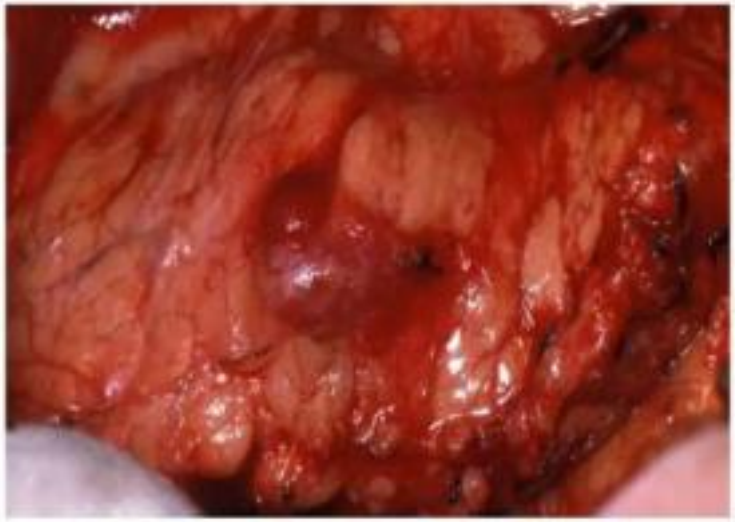
Whipple's Triad

- Fasting hypoglycemia (<2.2 mmol/L)
- Symptomatic hypoglycemia (autonomic and neuroglycemic symtoms)
- Relieve of symptoms after administration of glucose

When Whipple triad is mentioned, one classically thinks of insulinomas, but these features are not specific for insulinoma.

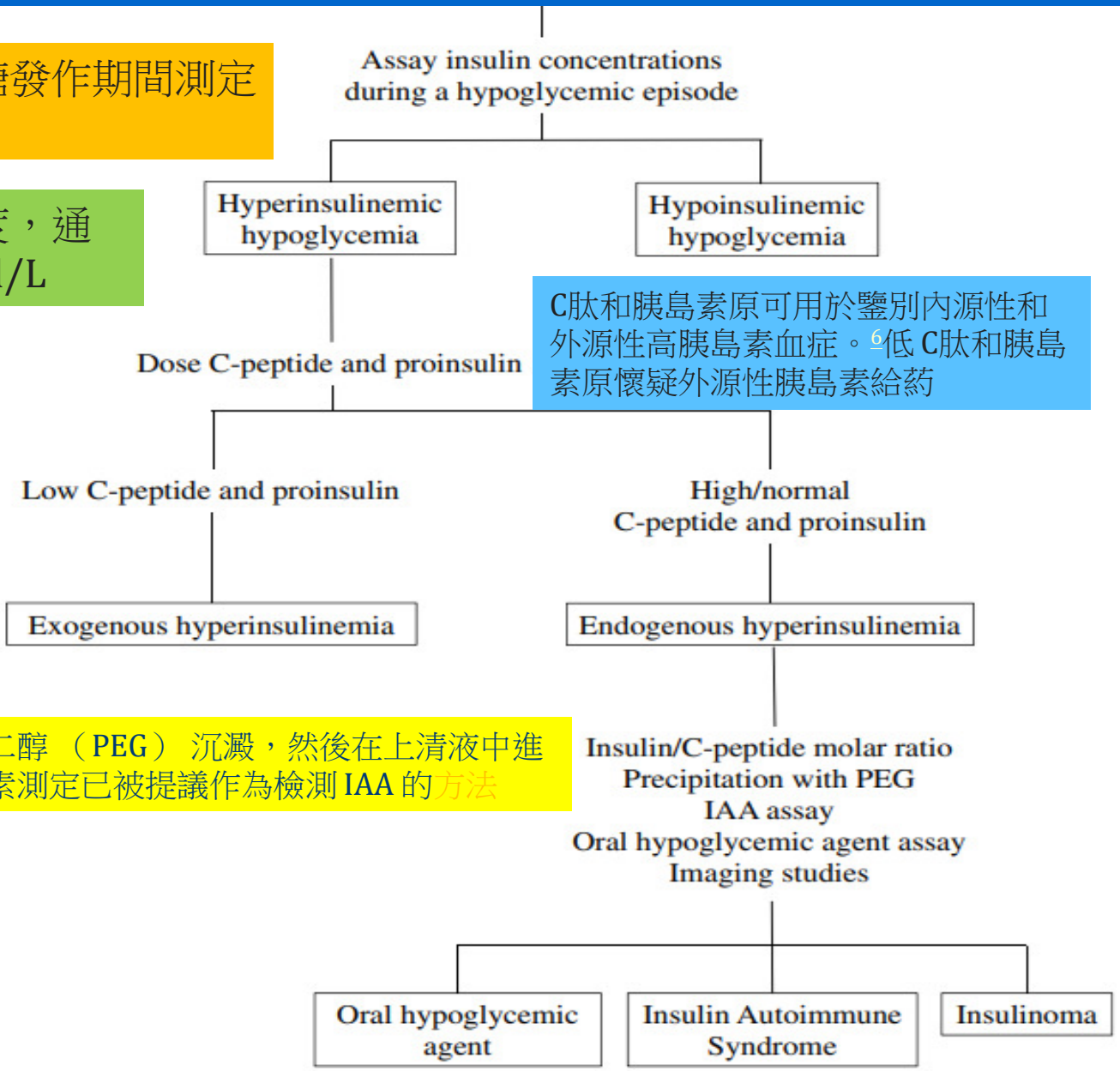
Insulinoma - a **rare islet tumor of the pancreas** that is characterized by **symptomatic hypoglycemia** and **inappropriately increased plasma insulin during an episode of spontaneous hypoglycemia**. Insulinomas are evenly distributed in the pancreas; that is one-third are found in the head, one-third in the body and one-third in the tail.

Management of insulinomas includes **controlling symptoms of hypoglycemia** and **surgical resection**. Hypoglycemia can be controlled through a combination of diet and medication.



第二步是在低血糖發作期間測定血清胰島素濃度。

極高的胰島素濃度，通常高於 1000 pmol/L



C肽和胰島素原可用於鑒別內源性和外源性高胰島素血症。[6]低 C肽和胰島素原懷疑外源性胰島素給葯

用聚乙二醇 （PEG） 沉澱，然後在上清液中進行胰島素測定已被提議作為檢測 IAA 的方法

Figure 2 Flowchart for the diagnosis of insulin autoimmune syndrome.
Abbreviations: PEG, polyethylene glycol; IAA, insulin autoantibodies.

- 1. As a consequence, a blood sample for the IAA assay should always be obtained in the suspect of IAS, even before proceeding to potentially useless and costly imaging examinations.
- 2. If IAA assay is not available, the sample should be preliminarily tested with PEG precipitation, and then eventually sent to a lab that owns the kit for measuring the IAA.
- Once the diagnosis of IAS has been confirmed, the patients should be evaluated carefully in order to assess the indication to pharmacologic therapy, always taking into account that no study have currently compared different treatment regimens.
- IAS patients should be monitored thoroughly, both during the active phase of the disease and following its remission. To date, even though the research in this field has accomplished astonishing results, there are still some missing points, especially regarding the **pathogenesis of the disease and its management**. The need for medical trials that compare different treatment modalities is urgent, even though the recruitment of a sufficient amount of IAS patients is difficult, due to the rarity of the condition

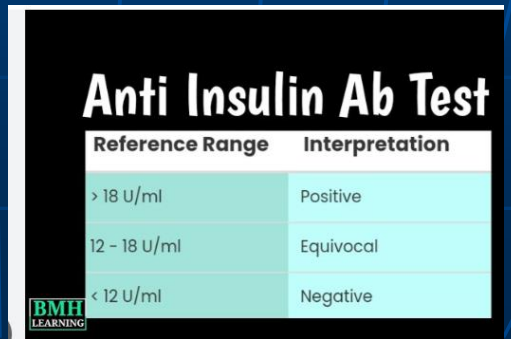
Treatment of IAS

- 1.在1970年至1992年間對197名被診斷患有IAS的患者進行修訂后，大約82%的IAS患者經歷了自發緩解,該系列列中低血糖發作的持續時間為1至3個月，性別無差異。
  2. 停用被確定為誘發 IAS 的藥物似乎是合理的

- 3.除了藥物治療外，還提出了飲食調整，以抵消低血糖發作的發展。合理的方法包括少食多餐，低碳水化合物含量，旨在減少餐后早期高血糖和隨之而來的胰島素分泌刺激，並預防低血糖發作。
- 4.用α-葡萄糖苷酶抑製劑（阿卡波糖）治療可預防餐后高血糖，因此在減少IAS血糖波動方面顯示出不同程度的益處。 alpha-glucosidase inhibitors (acarbose), prevents postprandial hyperglycemia, thus displaying different degrees of benefit in reducing glycemic excursions in IAS
- 5.在嚴重低血糖發作的情況下，可能需要靜脈注射葡萄糖，特別是為了防止夜間血糖波動。
- 6. strategies aimed at reducing insulin release, somatostatin analogues,[40,115] diazoxide[41,115,116] and even pancreatectomy[18,79] have been proposed, with variable results.
- 7. high-dose corticosteroids, with overall good results. Other immunosuppressive agents, such as azathioprine, have been proposed in case of persistency of the disease despite high-dose systemic corticosteroids. Rituximab is an anti-CD20 monoclonal antibody that has been used for the treatment of severe refractory IAS

IAS :Conclusion

- Fifty years following its first description, IAS has been extensively reported and many important results have been accomplished in the research regarding this condition.
- IAS is no longer considered a curious and rare disease mainly originating in Asian patients but has had a worldwide spread and its incidence seems definitely increasing, especially in western countries. This may be due to the wide diffusion of medications and substances that are well-known triggering factors in the pathogenesis of the disease, or to the larger awareness for this condition compared to the past decades.
- As a consequence, considering IAS in the differential diagnosis of hypoglycemia is nowadays mandatory, even outside the setting of patients of Asian ancestry.
- The diagnostic approach to IAS is complex, and the **gold standard for the differential diagnosis with other forms of hypoglycemia consists in the measurement of insulin autoantibodies.**



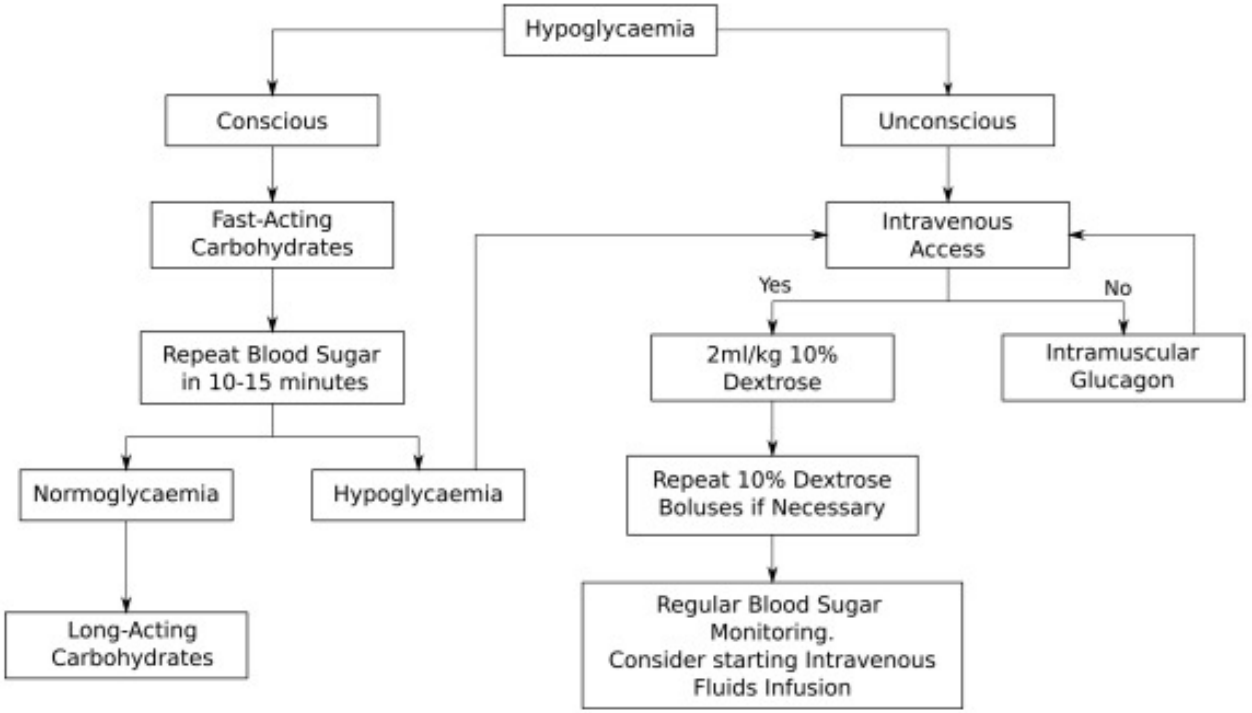


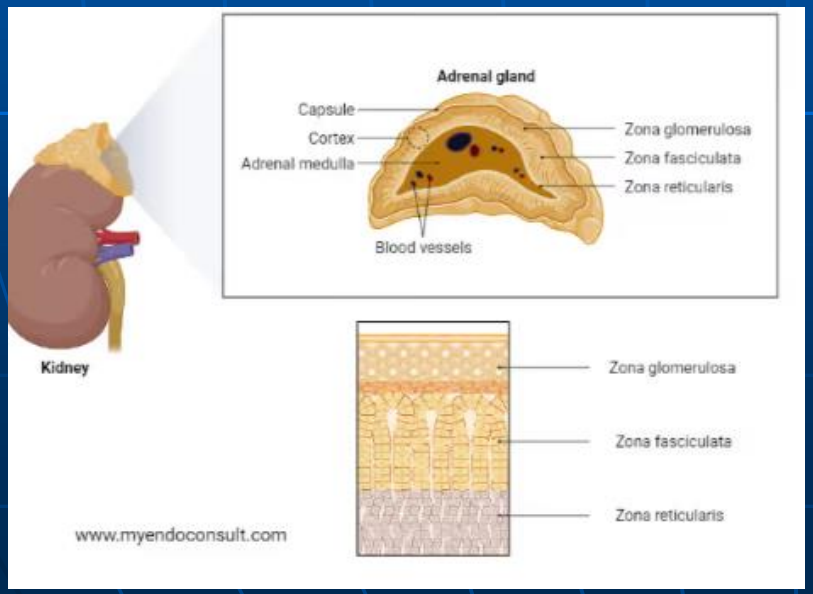
FIGURE 1
Emergency treatment of hypoglycaemia.

Shien Chen Lee [1], Elizabeth S Baranowski [2], Rajesh Sakremath et al **Hypoglycaemia in adrenal insufficiency** Front Endocrinol (Lausanne). 2023 Nov 20:14:1198519.

(L1095, L1096)

IV Hypoglycemia in adrenal insufficiency

- 腎上腺負責產生 3 種主要類固醇: 鹽皮質激素（主要是醛固酮）、糖皮質激素（主要是皮質醇）和雄激素。它們分別由腎上腺皮質的外腎小球帶、中束狀帶和網狀內帶產生. mineralocorticoids (mainly aldosterone), glucocorticoids (mainly cortisol) and androgens. These are produced by the outer zona glomerulosa, middle zona fasciculata and inner zona reticularis of the adrenal cortex respectively.
- 腎上腺皮質功能減退症 （AI） 發生在原發性腎上腺皮質功能衰竭或下丘腦-垂體軸中斷導致類固醇分泌不足時.



the outer zona glomerulosa, middle zona fasciculata and inner zona reticularis

Causes of Adrenal insufficiency

- primary, affecting the adrenal gland's ability to produce cortisol directly;
- secondary, affecting the pituitary gland's ability to produce adrenocorticotrophic hormone (ACTH);
- tertiary, affecting corticotrophin-releasing hormone (CRH) production at the level of the hypothalamus.

AI 有不同的臨床表現

- AI有不同的臨床表現。
- 患有 AI 的新生兒通常表現為嚴重低血糖、癲癇發作、生長遲緩、長期膽汁淤積性黃癉，在某些情況下還會出現昏迷。皮質醇缺乏導致膽汁酸合成轉運和成熟緩慢，導致結合型高膽紅素血症伴肝酶升高，通常在中位出生 13 日齡時出現 。
- 在患有 AI 的兒童和年輕人中，他們可能有低血糖、虛弱、疲勞、胃腸道癥狀、頭痛、肌肉和關節疼痛（1，2）。癥狀有時可能是非特異性的，例如體位性低血壓、暈厥、關節痛、厭食症和心理健康問題，
- 如未確診的艾迪生病病例報告所述，該病患者在崩潰狀態下到醫院就診（3）。
- 由於垂體和下丘腦異常而患有繼發性腎上腺皮質功能減退症（SAI）的個體可能會表現出涉及其他激素缺乏症的癥狀或同時存在中線缺陷。
- 如果他們伴有**生長激素（GH）缺乏**症，則低血糖的風險會增加，因為 GH 在低血糖中的反調節作用將在本文後面討論。

腎上腺危象(adrenal crisis)

- 腎上腺危象(adrenal crisis)是AI的一種危及生命的併發症，因為身體無法對生理壓力做出反應。
- 癥狀包括低血壓、脫水、嘔吐、腹痛，在最嚴重的情況下，它們可能表現為休克、昏迷和死亡 。
- 新生兒和兒童不明原因的猝死應引起對腎上腺危象的懷疑

在美國一項針對接受生長激素治療的患者的大型佇列研究中，發現 24.5%（433 人中有 106 人）的死亡是突然和意外的。這些意外死亡中有74%與多種垂體激素缺乏有關，在這106例死亡中，有31%的低血糖症被強調。此外，超過一半的意外死亡被認為患有未確診的繼發性腎上腺皮質功能減退症.

Mills JL, Schonberger LB, Wysowski DK, Brown P, Durako SJ, Cox C, et al.. Long-term mortality in the United States cohort of pituitary-derived growth hormone recipients. *J Pediatr* (2004) 144:430–6. (L1097)

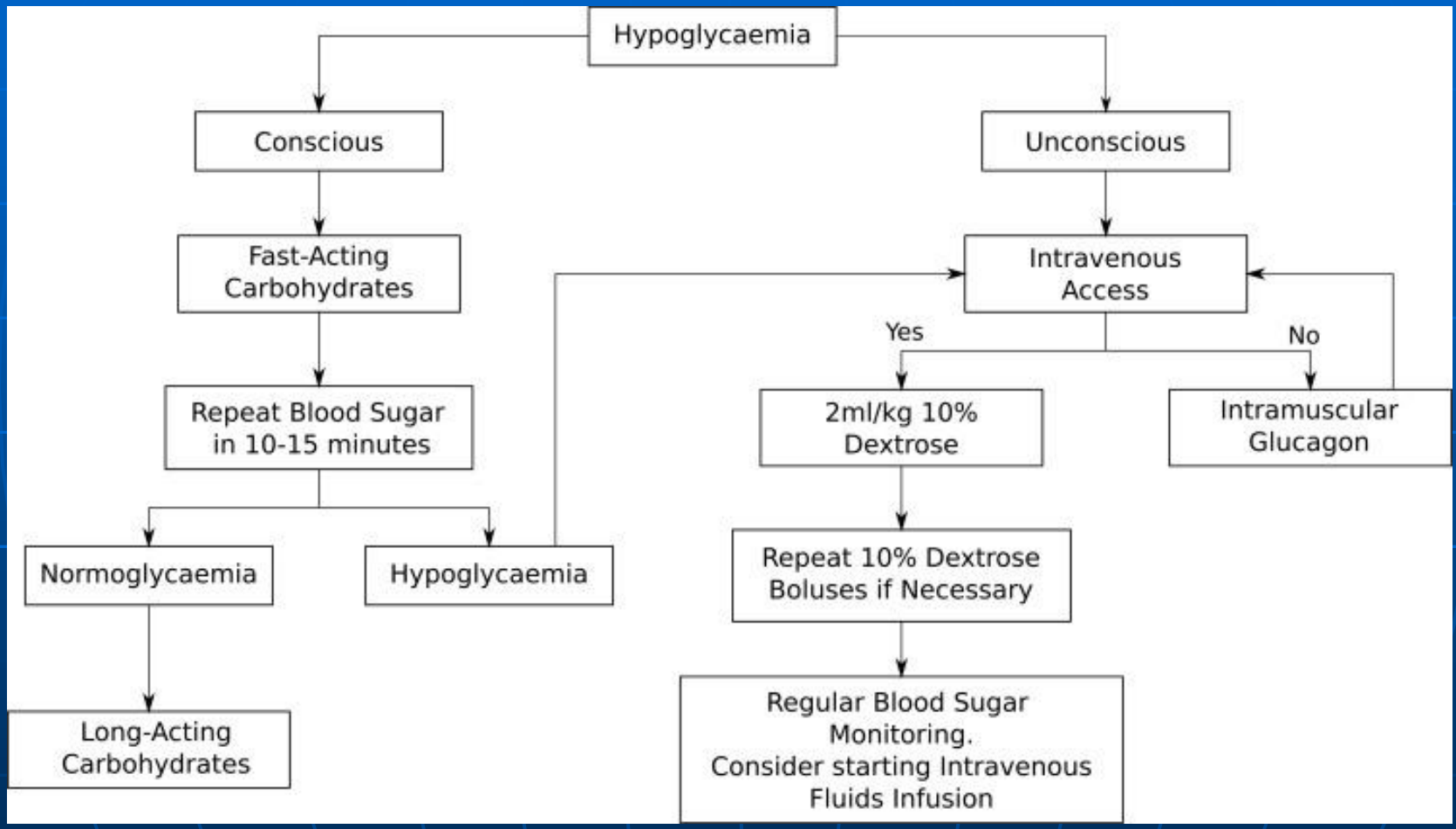
PAI

- 在法國進行的一項研究報告稱，165 名患有 PAI 的兒童和嬰兒中有 30 名 （18%） 出現低血糖發作。那些經歷過低血糖的人的基礎皮質醇水平顯著降低。

所有這些低血糖發作都與先前的禁食或嘔吐或病毒性疾病導致的經口攝入不足有關.

6 歲以下 CAH (先天性腎上腺皮質增生症)患兒的研究中，腎上腺危象的數量約為每 100 患者年 6.5 例.

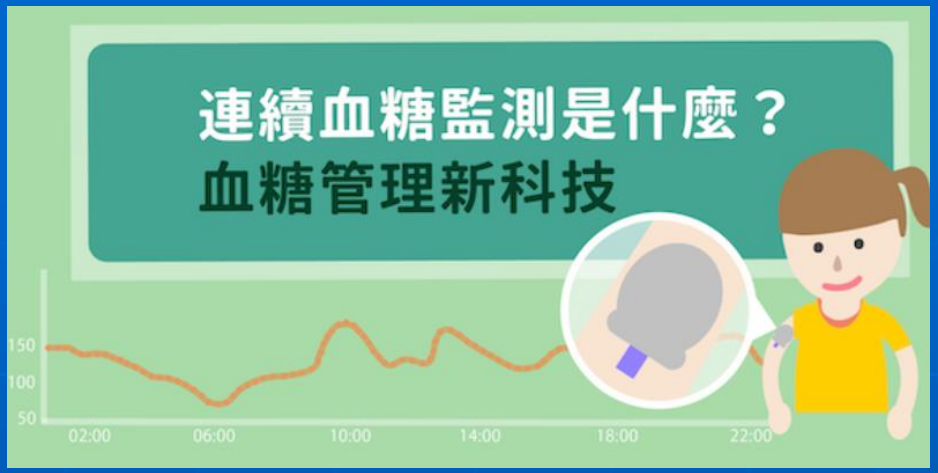
AI患者總是有腎上腺危象的風險。原發性或繼發性AI患者的腎上腺危象發生率約為每100患者年5-10例


Hypoglycaemia
Conscious
Unconscious
Fast-Acting Carbohydrates
Intravenous Access
Yes
No
Repeat Blood Sugar in 10-15 minutes
2ml/kg 10% Dextrose
Intramuscular Glucagon
Normoglycaemia
Hypoglycaemia
Repeat 10% Dextrose Boluses if Necessary
Long-Acting Carbohydrates
Regular Blood Sugar Monitoring. Consider starting Intravenous Fluids Infusion

連續血糖監測（CGM）之應用

- 連續血糖監測（CGM） 目前主要用於 1 型糖尿病患兒，較少用於使用胰島素的 2 型糖尿病患兒。
- 在患有 AI 的成年人中使用 CGM 進行的幾項研究顯示了益處，因為它們提供了有關血糖趨勢的有用資訊。
- 一項研究發現，每6名患有中樞性腎上腺功能減退症的成年人中，有5名患有中樞性腎上腺功能減退症，導致清晨頭痛。當根據 CGM 讀數改變患者氫化可的松的時間和劑量時，癥狀完全消退 .

- **目前僅在 1 型糖尿病中建立了使用技術進行兒童血糖監測的技術。未來的研究需要利用技術的進步來管理AI，並擴大CGM在AI兒童中的作用。同時，也許間歇性毛細血管或閃光血糖監測在檢測那些有低血糖風險的AI患兒方面可能是有益的，希望這將改善他們的神經發育結果並降低低血糖的死亡率。(L1096,L1095)**



self monitoring blood

	間接性掃描型, isCGM	即時型連續性, rtCGM
台灣機型	亞培 瞬感2 	美敦力 捍衛者 
心安診所 Xin an Clinic		
高低血糖警示	無/非即時	**有**
扎指尖血糖校正	不用。八小時內需要掃描兩次	需要
血糖紀錄間隔	每5分鐘；**每1分鐘**	每5分鐘
配戴時間	最長14天	最長7-10天
建議配戴適應症	1.**新診斷第二型**糖尿病 2.SMBG和A1C不吻合時 3.使用不會造成低血糖的藥物 4.願意一天掃描感應器好幾次 5.低血糖風險低，一天需要多次血糖數值	1.**第一型**、需要每日多次胰島素注射MDI、胰島素幫浦CSII 2.**懷孕時**期糖尿病 3.反覆低血糖、**低血糖無感** 4.血糖控制不佳、血糖波動大 5.高血糖危象、重症高血糖

連續血糖監測 CGM 健保給付規定 2017/3/1生效

糖尿病

- 第1型（有重大傷病證明）
- 新生兒糖尿病
- 近全胰臟切除所致

符合任1條件

- 血糖過度起伏、近6個月A1c ≥ 8%
- 低血糖無感症
- 常嚴重低血糖，須他人協助治療，近3個月有因低血糖至急診或住院
- 懷孕

給付規範

- 限地區醫院、區域醫院、醫學中心
- 限門診，需為住院患者前導
- 一年至多執行2次，且間隔3個月以上，若一年執行超過2次者，須事前審查
- 限糖尿病共同網醫療機構申報，執行人員和訓練醫師、管理師、衛教師必須參加過CGM之訓練課程

VII, Paraneoplastic syndrome

- Hypoglycemia is one of important manifestations of paraneoplastic syndrome.
- Causes (1) heavy consumption of energy by big tumors
- (2) Secretion of insulin-or insulin like substance by the tumor.

CONCLUSION

- hypoglycemia is characterized by a decrease in blood glucose levels <70 mg / dl
- Whipple's Triad
- Identification of cause to prevent recurrent hypoglicemia by anamnesis, physical examination and supportive investigation
- Drugs, particulary those used to treat diabetes or alcohol should be the first consideration. Other considerations include critical illness, hormone deficiencies and rarely non beta cell tumor
- In well individual, consider endogenous hyperinsulinism
- Urgent treatment → oral or parenteral therapy
- Identification of cause to prevent recurrent hypoglicemia

總結論: Treatment of hypoglycemia

GENERAL TREATMENT

- Immediate treatment should be focused on reversing the hypoglicemia.
- Stopping antidiabetic drugs and other drugs that cause hypoglycemia.
- If the patient is able to ingest simple glucose 15-20 grams (2-3 tablespoons of sugar) dissolved in water → eat or consume snacks if blood glucose stable
- Unable to ingest carbohydrate → parenteral glucose
- Evaluate the triggers for hypoglycemia

Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Dewasa di Indonesia. 2019

結論(2024.01.05)

1.hypoglycemia有很多原因,最常見的是糖尿病病人發生低血糖癥,可能是胰島素或低血糖藥劑過量

2.無糖尿病者發生低血糖癥有多種複雜的原因,必須審慎評估

- 3.藥物會發生自主免疫性低血糖癥值得注意.
- 4.低血糖癥必須迅速確認並治療.
- 5.低血糖癥必須確認發病之原因並尋求改善之方法

Suggested readings

- 1. Gurunanthan Palani [1], et al (Minnesota Univ.)**Clinical Presentation and Diagnostic**
- **Approach to Hypoglycemia in Adults Without Diabetes Mellitus**
- Endocr Pract. 2023 Apr;29(4):286-294.
- 2. American Diabetes Association Professional Practice Committee. Diabetes Care, 2022; 45(Suppl. 1): S46–S59.
- (L1062, 1063)
- 3. Agiostratidou, G, et al. Diabetes Care, 2017; 40(12): 1622–1630
- 4. Anthony L. McCall, David C. Lieb,Roma Gianchandani,et al : Management of Individuals With Diabetes at High Risk for Hypoglycemia: An Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology & Metabolism, 2023, 108, 529–562 .(L1064,L1065)