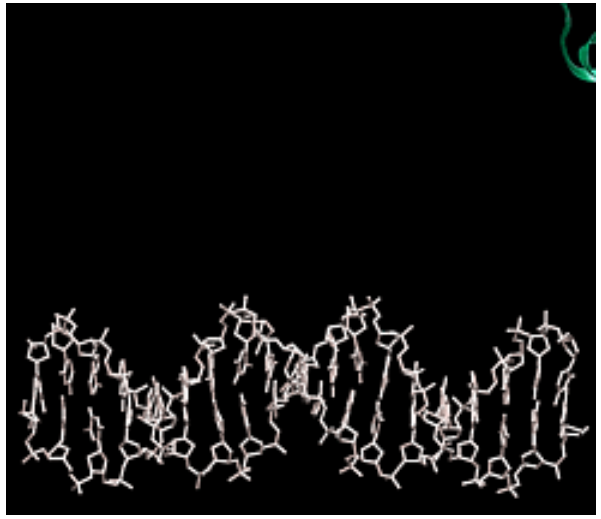

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Diabetes

Classification of Diabetes Mellitus by Etiology

- **Type 1** — β-cell destruction—complete lack of insulin

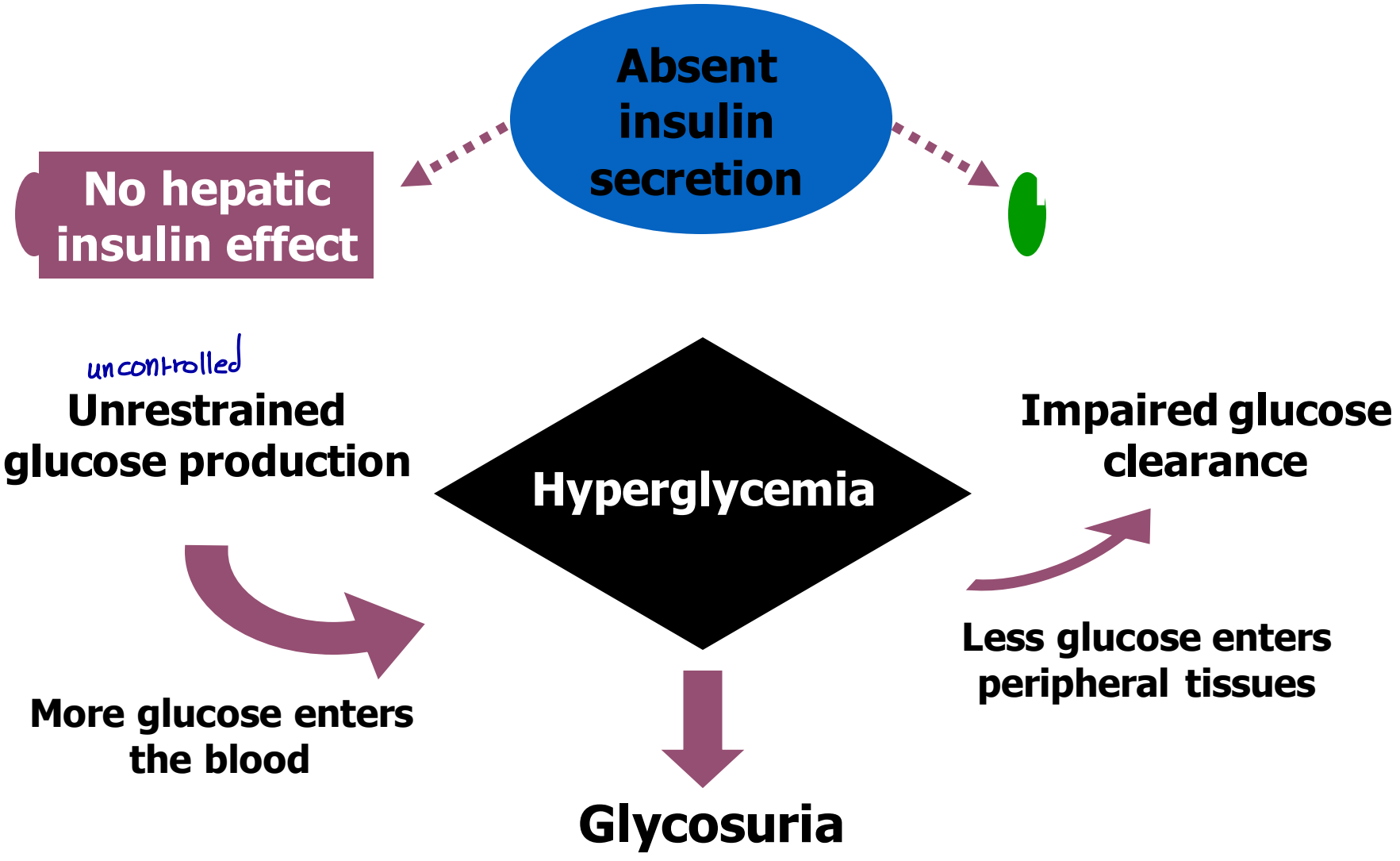
- **Type 2** — β-cell dysfunction and insulin resistance
  - Most common >90% of cases
  - ↳ loss of metabolic function of insulin on the target organs: liver, muscles, fat

Secondary Diabetes:

1. **Gestational** — β-cell dysfunction and insulin resistance during pregnancy
   - ↳ transient... pregnancy is a state of insulin resistance // genetic predisposition
     - ↳ to deliver enough quantity of nutrients to the growing fetus
2. **Other specific types**
   - Pancreatic diabetes. → Primary pathology from pancreas (chronic pancreatitis, pancreas malignancy)
     - Exocrine diseases of pancreas like cystic fibrosis
   - Endocrine Pathology predispose diabetes ← Endocrinopathies
     - ↳ hyperglycemia, cushing syndrome, acromegaly, growth hormone excess, pheocromocytoma
     - Thyrotoxicosis
   - Drug- or chemical-induced
     - ↳ steroid induced hyperglycemia
   - Other rare forms
     - ↳ Monogenic diabetes

Pathogenesis of Type 1 Diabetes : One Defect

↳ autoimmune destruction of Pancreatic β-cells



ISLET CELLS ANTIBODIES:

- A heterogeneous group of AB against a variety of cytoplasmic islet cell antigens — autoimmune markers important for diagnosis of type 1
- Not exclusively against *Beta* cells. Other islet cells are also targets. (so not reliable)
- Highly positive esp. in the pre- diabetic phase — in a while before hyperglyce-mia
- More positive at onset than later.
- Positivity decreases rapidly with duration of diabetes . — after diagnosis

ANTI GLUTAMIC ACID DECAROXYLASE (GAD) AB

+ve Anti GAD Antibodies

- **Present in 75- 84 % of recent onset DM type1.**

- Anti – ZnT8 antibodies → presents in 70% of diabetic pts. at time of diagnosis

D.M. Type 1

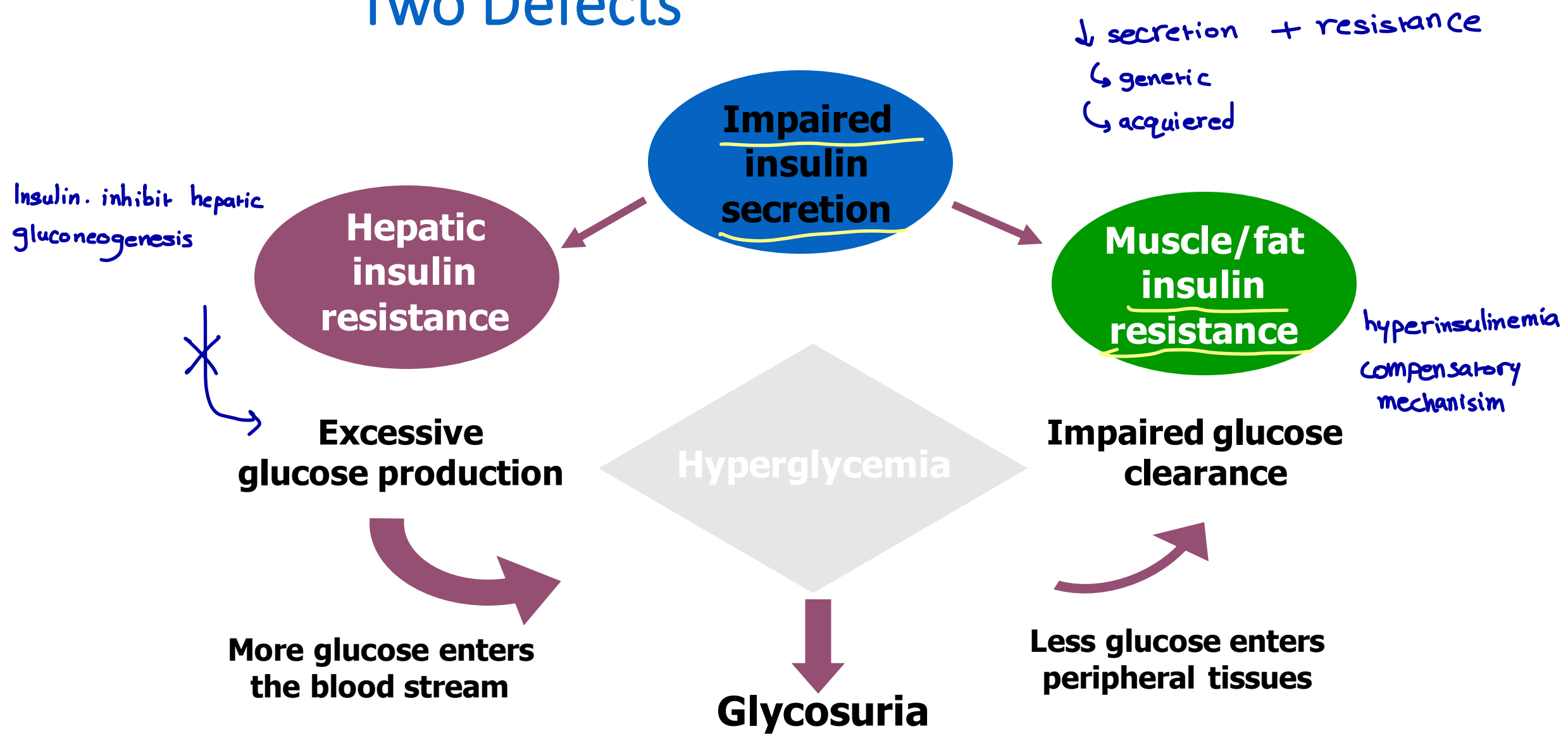
→ Viral infections: enteroviruses, respiratory viruses, Diet, immunization, stress

The combination of genetic ,environmental and autoimmune factors ultimately leads to β- cell destruction, which is an insidious process that may take up to 10 yrs before completion; once the β- cell mass is <5-10% of its original amount, symptoms of diabetes become manifest.

Genetic predisposition

ask about other autoimmune diseases:
↳ celiac disease
↳ vertigo
↳ autoimmune thyroid disease

Pathogenesis of Type 2 Diabetes : Two Defects



Type 2:

ROLE OF DIET, OBESITY, AND INFLAMMATION

- Increasing weight and less exercise
- Obesity epidemic
- Increasing T2DM in children and adolescents

MAJOR RISK FACTORS (Type2 DM)

- FH of DM , obesity (abdominal obesity (visceral adiposity)
- Overweight (BMI > 25 kg/m2)
-physical inactivity
-Race/ethnicity (African-Americans, Hispanic-Americans)
- History of IFG or IGT
  - ↳impaired fasting glucose
  - ↳impaired glucose tolerance
-History of GDM or delivery of a baby weighing >4.5 kg
  - ↳carries risk of diabetes
-Signs of insulin resistance or conditions associated with insulin resistance:
  - Hypertension (140/90 mmHg in adults)
  - HDL cholesterol 35 mg/dl and/or a triglyceride level 250 mg/dl
    - hyperlipidemia
  - Polycystic ovary syndrome
  - acanthosis nigricans
    - ↳ hyperpigmentation at the back of the neck

Metabolic syndrome (syndrome X)

Insulin resistance signs: Obese (abdomin) → waist circumference
(type 2)
acanthosis nigricans

↳ Non alcoholic fatty liver disease (related with obesity)

Type 1 versus type 2 diabetes

↳ polygenic diabetes

1 Body habitus :T2DM: overweight.T1DM:lean

2 Age :T2DM :after puberty.

T1DM 4 -6 yrs and 10 -14 yrs of age

3 Insulin resistance :T2DM: acanthosis nigricans, HTN, dyslipidemia, and PCOS

4 FH: (+) in both type 2 > type 1

5 T1DM is suggested by +:GAD, tyrosine phosphatase (IA2), and/or insulin Abs

Up to 30 % of T2DM have + Abs

Increasing obesity prevelance

LADA → T1DM in pr. >35 for e.g.> Require insulin

Latent autoimmune diabetes

MODY

Monogenic , rare AD disease

- MODY is non-insulin requiring form of diabetes,occurring in children and young adults,resulting from genetic defect in beta-cell function,and inherited in autosomal dominant trait(AD)

20, 21 y/o

→ family history of DM (grandfather has DM, controlled with sulfonylureas

MODY

MATURITY ONSET DIABETES OF THE YOUNG (MODY)

↳ defective insulin secretion (no lack of insulin)

- Clinical presentation partly similar to type 2 DM but occurring in young age group-mostly adolescents

- Autosomal dominant inheritance; 5 different gene defects described

- All relatively rare.

↳ respond well to insulin secretagogues

Clinical Features

	Obesity	Insulin resistance	Autoimmunity
Type 1	No غالبًا	No	Yes
Type 2	Yes	Yes	No
MODY	No	No	No

Gestational Diabetes

- Hyperglycemia during pregnancy—usually resolves after birth
- High risk of perinatal morbidity and mortality

Gestational Diabetes

- High risk of later type 2 diabetes in both mother and baby.
- Diagnosed by specific oral glucose tolerance test methods.
- Requires intensive dietary and glycemic management.

↳ Complications: Microsomia, pre-term delivery

سوائل زيادة
حول الجنين

Oral glucose tolerance test for a pregnant women:

at 0 hour → 92

after 1 hour → 180

after 2 hours → 153

Symptoms

Classical symptoms of hyperglycemia: (osmotic symptoms)

- Polyuria, increased frequency of urination, nocturia.
- Increased thirst, and dry mouth
- Weight loss

polydepsia, polyphagia

- Blurred vision
- Numbness in fingers and toes
- Fatigue
- Impotence (in some men)

diabetic retinopathy

diabetic neuropathy

Signs

- Weight loss: muscle weakness
- Decreases sensation
- Loss of tendon reflexes
- Foot Inter-digital fungal infections
- Retinal changes by fundoscopy

Criteria for the diagnosis of diabetes

1. **A1C ≥6.5 percent**. Glycated hemoglobin (blood glucose average in the last 3 months)
   5.7 – 6.4 → prediabetes
2. **FPG ≥126 mg/dL** . Fasting is defined as no caloric intake for at least 8 hr. ↳fasting plasma glucose
   100 – 125 → prediabetes
   < 100 → normal
3. **Two-hour plasma glucose ≥200 mg/dL** during an OGTT. 75 g anhydrous glucose dissolved in water.
   140 – 199 → prediabetes
   < 140 → normal
4. In a patient **with classic symptoms** of hyperglycemia or hyperglycemic crisis, **a random plasma glucose ≥200 mg/d**L .

* In the absence of unequivocal **symptomatic** hyperglycemia, criteria 1-3 should be confirmed by repeat testing.

Repeat abnormal test

Management of diabetes

1. Lifestyle modifications:
- Medical nutrition therapy
- increased physical activity
- weight reduction
2. Oral Drug Therapy/Noninsulin SC therapy
3. Insulin therapy