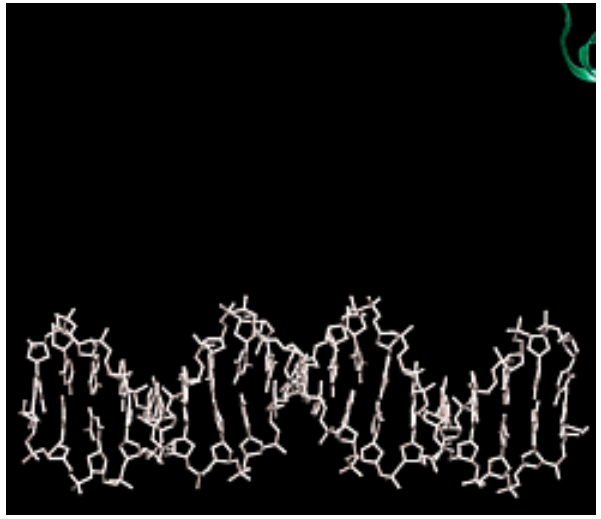

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Diabetes

Classification of Diabetes Mellitus by Etiology

- **Type 1** β-cell destruction—complete lack of insulin
- **Type 2** β-cell dysfunction and insulin resistance

Pregnancy is a state of insulin resistance

- **Gestational** β-cell dysfunction and insulin resistance during pregnancy

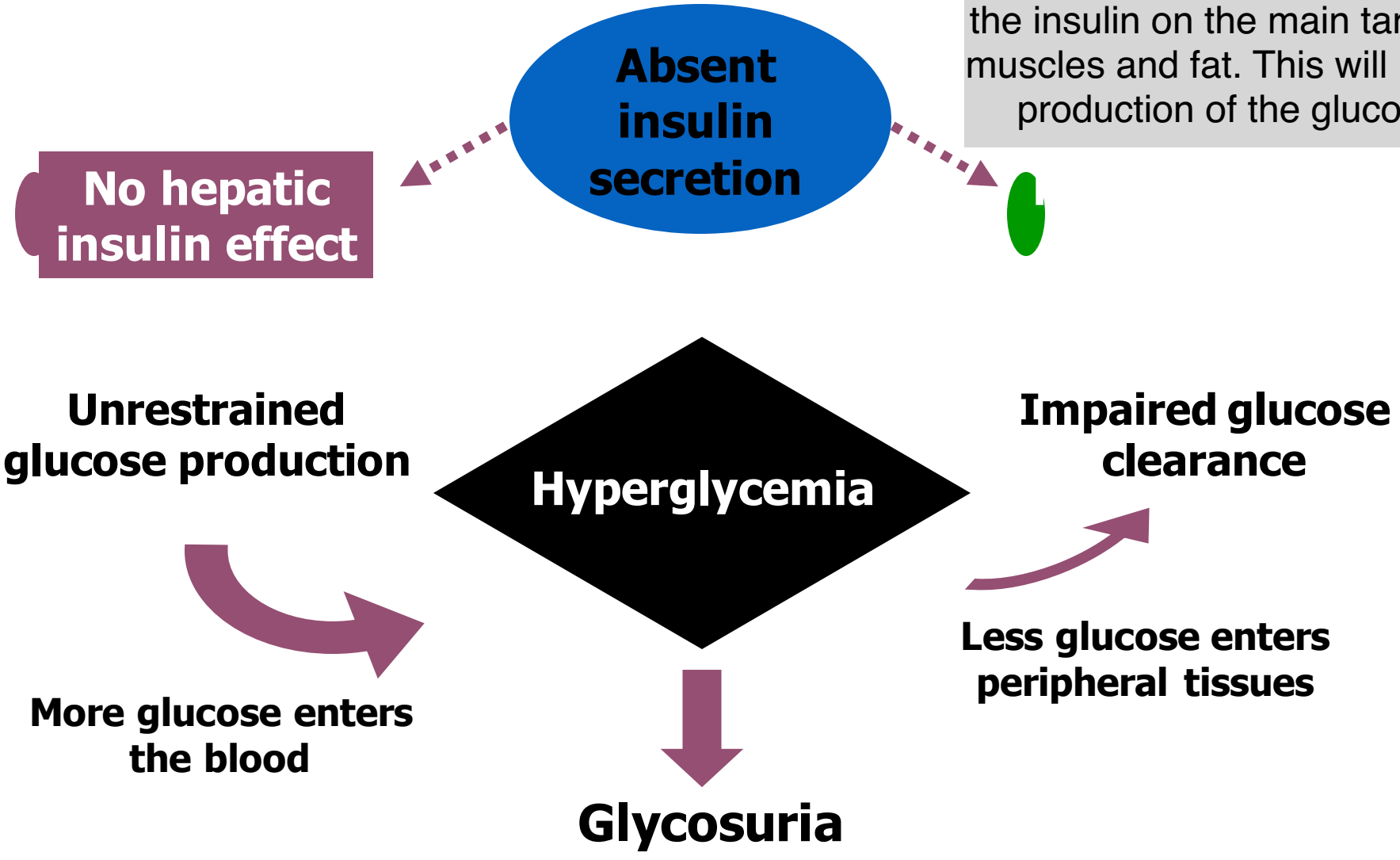
Transient (that's what we hope for, we're afraid of persistent diabetes)

- **Other specific types** (Secondary diabetes)
  - **Pancreatic diabetes.** Chronic pancreatitis, pancreatic malignancy, also exocrine disease of the pancreas (cystic fibrosis)
  - **Endocrinopathies** Cushing syndrome, acromegaly, thyrotoxicosis, growth hormone excess, pheochromocytoma
  - **Drug- or chemical-induced** Steroid-induced hyperglycemia (cortisol)
  - **Other rare forms**

The reason why some females have gestational diabetes and others don't is because this mother can have genetic predisposition for insulin resistance, it stays hidden until a super imposing factor shows up and increases the insulin resistance leading to hyperglycemia

Pathogenesis of Type 1 Diabetes : One Defect

Complete lack of insulin due to autoimmune destruction of the B cells There's loss of the metabolic function of the insulin on the main target organs: liver, muscles and fat. This will lead to increased production of the glucose by the liver



ISLET CELLS ANTIBODIES:

Antibodies against one or more of the islet cell components, these antibodies helps us in confirming the diagnosis

If there's a patient with one or more siblings have DM, we can do screening for our patient (their sibling) even if he/she has normal glucose levels, there might be elevated autoimmune markers

This stage is called pre-clinical stage of type 1 DM

- **A heterogeneous group of AB against a variety of cytoplasmic islet cell antigens**
- **Not exclusively against *Beta* cells. Other islet cells are also targets.** There's also anti GAD antibodies (glutamic acid decarboxylase)
- **Highly positive esp. in the pre- diabetic phase** asymptomatic
- **More positive at onset than later.**
- **Positivity decreases rapidly with duration of diabetes .**

These antibodies will be positive before a while of the presentation of hyperglycemia some patients can be diagnosed depending on those autoimmune markers

Positivity/ titer level will decrease overtime (after the diagnosis of diabetes)

ANTI GLUTAMIC ACID DECAROXYLASE (GAD) AB

Anti GAD Antibodies

One of the enzymes responsible for the insulin synthesis and secretion

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

D.M. Type 1

Since it's an autoimmune disease, we ask the patient if she/he has other autoimmune disease and we ask about the family history of autoimmune diseases

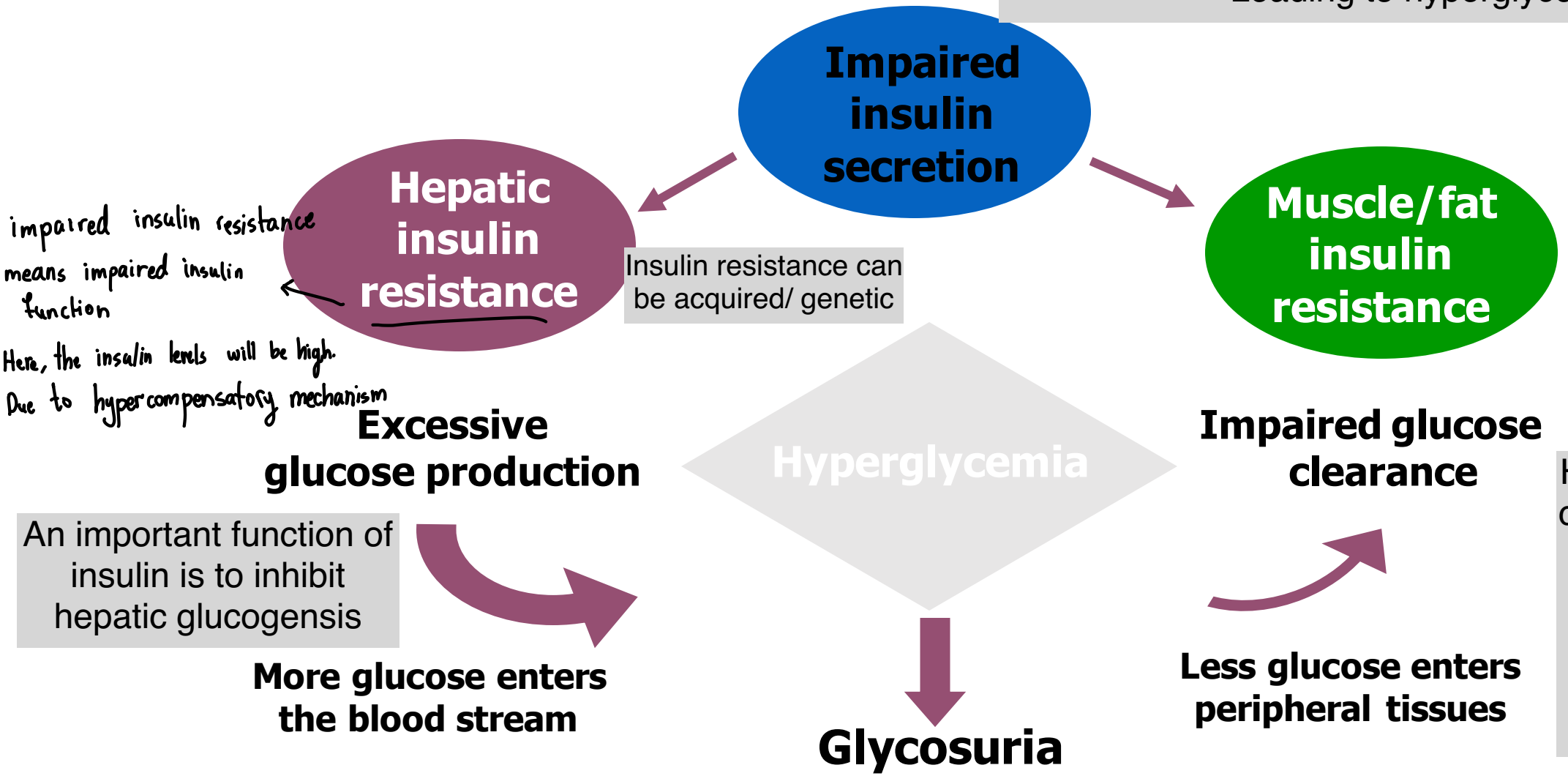
The combination of genetic ,environmental and autoimmune factors ultimately leads to β- cell destruction, which is an insidious process that may take up to 10 yrs before completion; once the β- cell mass is <5-10% of its original amount, symptoms of diabetes become manifest.

Common autoimmune diseases in diabetic patients: celiac disease, vitiligo, thyroid disease, Addison disease

Also there would be ZnT8 antibody, up to 70% positive in type 1 DM at the time of diagnosis

Pathogenesis of Type 2 Diabetes : Two Defects

Relative insulin deficiency with relative insulin resistance (combination of both with variable degrees)
Leading to hyperglycemia



This hyperglycemia can affect insulin secretion

Hyperglycemia can cause glucotoxicity, this can lead transient pancreatic shutdown/ exhaustion

ROLE OF DIET, OBESITY, AND INFLAMMATION

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

And young adults

The obesity makes the diabetes less clear to diagnose

MAJOR RISK FACTORS (Type2 DM)

- FH of DM Remember: Family history in both types of diabetes is important
- Overweight (BMI > 25 kg/m2) Because it causes insulin resistance (visceral/ abdominal adiposity)
-physical inactivity
-Race/ethnicity (African-Americans, Hispanic-Americans)
- History of IFG or IGT Impaired fasting glucose or impaired glucose tolerance
-History of GDM or delivery of a baby weighing >4.5 kg

Gestational

-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
  - *Polycystic ovary syndrome
  - *acanthosis nigricans

Diagnosis of insulin resistance is clinical

Metabolic syndrome
High blood pressure, excess body fat around the waist, high blood sugar, abnormal cholesterol or triglyceride levels. Others (PCOS, NAFLD)

insulin resistance test

HOMA-IR tells you how much insulin your body needs to keep your blood sugar levels in check. This test was designed to measure insulin resistance, an early stage of type 2 diabetes that increases your risk of many chronic diseases.

Type 1 versus type 2 diabetes

Type 1 DM can also happen in young adults
LADA (latent autoimmune diabetes in adults), the reason why it got delayed in showing is because of the environmental factors

1 Body habitus :T2DM: overweight.T1DM:lean

LADA : lean body habitus Treatment: they'll need insulin

2 Age :T2DM :after puberty. 50 60 year

You can also see an obese child with type 1 DM since we have increased prevalence of obesity in all ages

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

In young adults we test the antibody for them

Up to 30 % of T2DM have + Abs

MODY

Polygenic: type 2 diabetes
Monogenic: rare autosomal dominant 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)

There's a defect in insulin secretion

MODY

MATURITY ONSET DIABETES OF THE YOUNG (MODY)

- 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.

Responds well to insulin secretagogues, ex: sulfonylureas

Clinical Features

	Obesity	Insulin resistance	Autoimmunity
Type 1	No	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 glucose tolerance test methods.
- Requires intensive dietary and glycemic management.

Oral test

You give the patient glucose (around 100 grams) and then re-do the test after 2 hours

Symptoms

Classical symptoms of hyperglycemia also known as osmotic symptoms

- Polyuria, increased frequency of urination, nocturia.
- Increased thirst, and dry mouth
- Weight loss
- Blurred vision
- Numbness in fingers and toes
- Fatigue
- Impotence (in some men)

Polydipsia, polyphagia and weight loss

We say weight loss symptom when we reach catabolic state (in absolute or non absolute insulin deficiency) not in insulin resistance

Even from hyperglycemia or due to diabetic neuropathy

Due to 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

Very important slide

Glycated Hb

1. **A1C ≥6.5 percent**. Pre-diabetic: from 5.7 - 6.4
2. **FPG ≥126 mg/dL** . Fasting is defined as no caloric intake for at least 8 hr. Fasting plasma glucose Pre-diabetic: 100-125 mg/dl Normal: less than 100mg/dl
3. **Two-hour plasma glucose ≥200 mg/dL** during an OGTT. 75 g anhydrous glucose dissolved in water. Oral glucose tolerance test Pre-diabetic: 140 - 199 mg/dL Normal: less than 140mg/dL
4. In a patient **with classic symptoms** of hyperglycemia or hyperglycemic crisis, **a random plasma glucose ≥200 mg/dL** .

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

If asymptomatic, repeat test twice for confirmation of diagnosis

Management of diabetes

1. Lifestyle modifications:

- Medical nutrition therapy
- increased physical activity
- weight reduction

2. Oral Drug Therapy/Noninsulin SC therapy

3. Insulin therapy

Subcutaneous