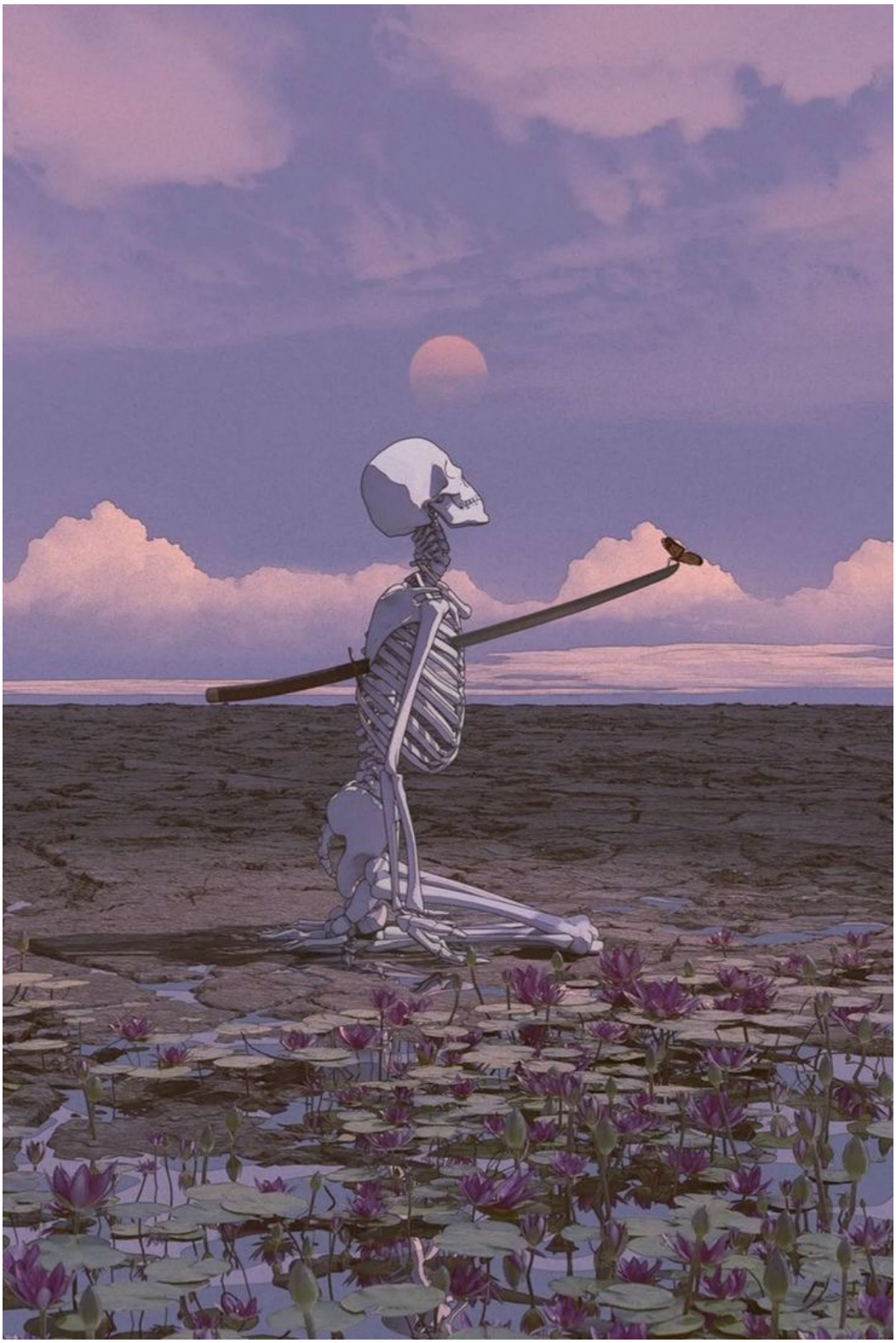


Diabetes mellitus

The History of Diabetes mellitus

❑Approximately 1550BC an Egyptian manuscript mentions a rare disease that causes the patient to lose weight rapidly and urinate frequently. This is thought to be the first reference to diabetes.

❑Around the 11 th Century, Some physicians taste the urine, and diabetes is given its second name mellitus, meaning 'sweet as honey' in Latin.

❑Diabetes mellitus is taken from the Greek word diabetes, meaning siphon - to pass through and the Latin word mellitus meaning sweet.

❑In 1922 Banting, Best, and Collip purified the hormone insulin from the pancreas of cows at the University of Toronto, leading to the availability of an effective treatment for diabetes in 1922.

❑Over the years, exceptional work has taken place, and multiple discoveries, as well as management strategies, have been created to tackle this growing problem.

❑Unfortunately, even today, diabetes is one of the most common chronic diseases in the country and worldwide.

PREVALENCE

❑Diabetes is estimated to affect > 500 millions adults worldwide, with a global prevalence of 10.5% among adults.

❑Type 2 diabetes accounts for 90-95% of cases of diabetes worldwide.

❑The prevalence of type 2 diabetes has risen alarmingly in the past decade, linked to the trends in obesity and sedentary lifestyle.

❑Given the marked increase in childhood obesity, there is concern that the prevalence of diabetes will continue to increase substantially.

❑Type 1 diabetes accounts for another 5 to 10% of the cases.

❑Known monogenic causes of diabetes represent a small fraction of cases.

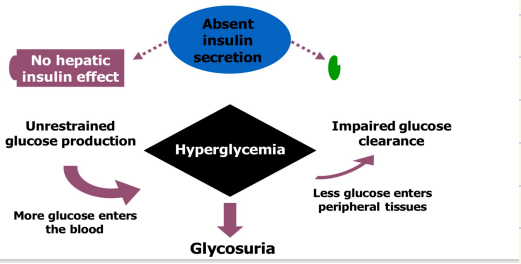
Classification of Diabetes Mellitus by Etiology

Type 1 autoimmune destruction of the beta cells (type 1A)

nonautoimmune islet destruction (type 1B)

- Type 2 ?-cell dysfunction and insulin resistance
- Gestational ?-cell dysfunction and insulin resistance during pregnancy
- Other specific types
- Pancreatic diabetes.
- Endocrinopathies
- Drug- or chemical-induced
- Other rare forms

Pathogenesis of Type 1 Diabetes : One Defect



Type 1A diabetes:

➢Autoimmune destruction of the insulin-producing beta cells in the islets of Langerhans leading to absolute insulin deficiency.

➢Occurs in genetically susceptible subjects, triggered by one or more environmental agents, and usually progresses over many months or years during which the subject is asymptomatic and euglycemic.

❑Genetic susceptibility :Polymorphisms of multiple genes are known to influence the risk of type 1A diabetes.

❑Target autoantigens : There are a number of autoantigens within the pancreatic beta cells play important roles in the initiation or progression of autoimmune islet injury including: glutamic acid decarboxylase (GAD), insulin, insulinoma-associated protein 2 (IA-2), and zinc transporter ZnT8.

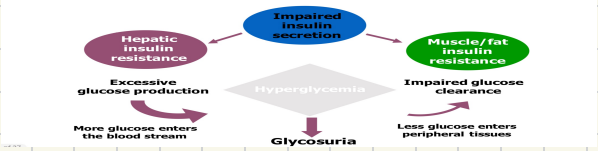
❑Environmental factors include pregnancy-related and perinatal influences, viruses, and ingestion of cow's milk and cereals.

Type 1B or "idiopathic" diabetes:

➢Some patients with absolute insulin deficiency have no evidence of autoimmunity and have no other known cause for beta cell destruction.

➢Presence of nonautoimmune pathophysiologic processes leading to near-complete loss of beta cell function.

Pathogenesis of Type 2 Diabetes : Two Defects



Pathogenesis of type 2 diabetes mellitus

❑Multifactorial

❑Type 2 diabetes is a polygenic disease, with complex interaction between genetic and environmental factors contributing to disease risk.

❑Patients typically present with a combination of varying degrees of insulin resistance and defective insulin secretion (beta cell dysfunction).

• Insulin resistance :
Attributed to predominantly "environmental" factors related to overeating, sedentary lifestyle, and resulting overweight and obesity, with
less prominent contributions from aging and genetics.
• Impaired insulin secretion:
Resulting from genetic influences and the programming of the beta cell
mass and function in utero.
• Hyperglycemia itself can impair pancreatic beta cell function and exacerbate insulin resistance ("glucotoxicity"), leading to a vicious cycle
of hyperglycemia causing a worsening metabolic state.

Monogenic diabetes (formerly called maturity onset diabetes of the young)

• Diabetes diagnosed at a young age (<25 years)
• Autosomal dominant transmission and lack of autoantibodies.
• MODY is the most common form of monogenic diabetes, accounting for 2
to 5% of diabetes.
• Many patients are misclassified as having either type 1 or 2 diabetes.
• The original MODY nomenclature ("MODY1," "MODY2," "MODY3," etc) has
bee replaced by the term "monogenic diabetes" with the name of the
gene associated with the trait.

• The involved genes control pancreatic beta cell development,
function, and regulation. And the mutations in these genes cause
impaired glucose sensing and insulin secretion with minimal or no
defect in insulin action.
• Mutations in hepatocyte nuclear factor-1-alpha (HNF1A,50-65%) and
the glucokinase
(GCK,15-30%) genes are the most commonly identified.

Latent autoimmune diabetes in adults (LADA)

• Diagnosis :
• An adult-onset diabetes who are positive for at least one islet autoantibody
with prolonged preservation of insulin secretion.
• LADA may be considered a slowly progressive variant of type 1 diabetes.
Patients with LADA are a heterogeneous group with variable titers of
antibodies, body mass index (BMI), and rate of progression to insulin
dependence.
• Adults with LADA may not require insulin treatment at diagnosis but typically
progress to insulin dependence after several months to years.
• The presence and degree of elevation of anti-GAD or anti-ICA antibodies can
help predict accelerated disease progression, an earlier requirement for
insulin therapy, subtherapeutic responses to oral hypoglycemic medications,
and greater risk of ketoacidosis.
• Genetics.In genotyping analyses, LADA shares genetic features of both type
1 and type 2 diabetes.

Gestational Diabetes

❑Occurs when a woman's pancreatic function is insufficient to overcome the insulin resistance associated with the pregnancy state (placental secretion of diabetogenic hormones)
❑Develops in the second or third trimester and usually resolves after birth.
❑High risk of perinatal morbidity and mortality

❑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.

Clinical features distinguishing type 1 diabetes, type 2 diabetes, and monogenic diabetes*

Clinical features	Type 1 diabetes mellitus	Type 2 diabetes mellitus	Monogenic diabetes
Age of diagnosis (years)	Majority <25, but may occur at any age	Typically >25 but incidence is increasing in adolescents, paralleling increasing rates of obesity in children and adolescents¶	<25
Weight	Usually thin, but with obesity epidemic overweight and obesity at diagnosis becoming more common	>90% at least overweight	Similar to general population
Autoantibodies	Present	Absent	Absent
Insulin dependent	Yes	No	No
Insulin sensitivity	Normal when controlled	Decreased	Normal (may be decreased if obese)
Family history of diabetes	Infrequent (5 to 10%)	Frequent (75 to 90%)	Multigenerational, ie, ≥3 generations
Risk of diabetic ketoacidosis	High	Low	Low

Major Risk Factors (Type2 DM)

Categories of increased risk for diabetes (prediabetes)*

FPG 100 to 125 mg/dL (5.6 to 6.9 mmol/L) – IFG
2-hour post-load glucose on the 75 g OGTT 140 to 199 mg/dL (7.8 to 11.0 mmol/L) – IGT
A1C 5.7 to 6.4% (39 to 46 mmol/mol)

Medical conditions associated with an increased risk of type 2 diabetes
including:
1. Gestational diabetes
2. Polycystic ovary syndrome
3. Metabolic syndrome

Obesity

❑Obesity is the most important modifiable risk factor for type 2 diabetes.
❑Inducing resistance to insulin-mediated peripheral glucose uptake.
❑The mechanism by which obesity induces insulin resistance is poorly
understood.
❑Reversal of obesity decreases the risk of developing type 2 diabetes and
improves glycemic management and can lead to remission in diabetic
patients.

❑The degree of insulin resistance and the incidence of type 2 diabetes
are highest in those with central or abdominal obesity, as measured by
waist circumference.
❑Intra-abdominal (visceral) fat rather than subcutaneous or
retroperitoneal fat appears to be of primary importance.
❑Why the pattern of fat distribution is important and the relative roles of
genetic and environmental factors in its development are not known!

Family history/Genetic susceptibility

❑The risk is likely mediated through genetic, anthropometric (BMI and waist
circumference), and lifestyle (diet, physical activity, smoking) factors.
❑Any first degree relative ..... 2X-3X increase risk of developing DM.
❑With both a maternal and paternal history of type 2 diabetes...5X-6X
increase risk of DM .
❑Insulin resistance and impaired insulin secretion in type 2 diabetes have a
substantial genetic component.

Lifestyle factors

❑ Insulin resistance and impaired insulin secretion can be influenced, both
positively and negatively, by behavioral factors, such as physical activity,
diet, smoking, alcohol consumption, body weight, and sleep duration.
Improving these lifestyle factors can reduce the risk of diabetes mellitus

Exercise

❑A sedentary lifestyle lowers energy expenditure, promotes weight gain, and
increases the risk of type 2 diabetes .
❑ Among sedentary behaviors, prolonged television watching is consistently
associated with the development of obesity and diabetes.
❑Physical inactivity, even without weight gain, appears to increase the risk of
type 2 diabetes.
❑Physical activity of moderate intensity reduces the incidence of new cases of
type 2 diabetes, regardless of the presence or absence of IGT.

Smoking

• Several large prospective studies have raised the possibility that cigarette
smoking increases the risk of type 2 diabetes.
• Secondhand smoke also increases the risk.
• While a definitive causal association has not been established, a relationship between cigarette smoking and diabetes mellitus is biologically possible based upon a number of observations:
1. Smoking increases the blood glucose concentration after an oral glucose
challenge.
2. Smoking may impair insulin sensitivity.
3. Cigarette smoking has been linked to increased abdominal fat distribution.

Dietary patterns

Adherence to a diet high in fruits, vegetables, nuts, whole grains, and olive
oil is associated with a lower risk of type 2 diabetes

CLINICAL PRESENTATION

Type 2 DM:

❑The majority of patients are asymptomatic at presentation, with
hyperglycemia noted on routine laboratory evaluation.
❑The frequency of symptomatic diabetes has been decreasing in parallel with
improved efforts of screening.
❑The classic symptoms of hyperglycemia (including polyuria, polydipsia,
nocturia, blurred vision, and weight loss) are often noted only in retrospect
after high blood glucose reading.
❑DKA as the presenting symptom of type 2 diabetes is uncommon but may
occur under certain circumstances (usually severe infection or other acute
illness).
❑Hyperosmolar hyperglycemic state (marked hyperglycemia, severe
dehydration, and obtundation, but without ketoacidosis) is rare.

Type 1 DM

❑DKA is the initial presentation in about 25% of adults with newly
diagnosed type 1 diabetes.
❑More common in children than in adults with type 1 DM

American Diabetes Association criteria for the diagnosis of diabetes

1. A1C ≥6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR
2. FPG ≥126 mg/dL (7 mmol/L). Fasting is defined as no caloric intake for at least 8 hours.*
OR
3. 2-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).

Management of diabetes

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

TREATMENT GOALS

1- Diabetes Education : instruction on nutrition, physical activity, optimizing metabolic control, and preventing complications.
2- Evaluation for micro- and macrovascular complication
3- Attempts to achieve near normoglycemia
4- Minimization of cardiovascular and other long-term risk factors
5- Avoidance of drugs that can exacerbate abnormalities of insulin or lipid metabolism.

Diabetes Education
Intensive lifestyle modification
Intensive behavioral modification interventions including weight
reduction and increasing activity levels are successful in
- **Reducing weight**
- **Improving glycemic management**
- **Reducing the need for glucose-lowering medications.**

1- Medical nutrition therapy
Aiming for weight reduction or at least weight maintenance.
2- Weight reduction
- By diet control, pharmacological or surgical therapy.
- Improved glycemic state is induced by weight loss through partial
correction of the two major metabolic abnormalities in type 2 diabetes:
insulin resistance and impaired insulin secretion.
- Weight loss and weight loss maintenance supports all effective type 2
diabetes therapy and reduces the risk of weight gain associated with
sulfonylureas and insulin.

3- Exercise
- Regular exercise is beneficial for diabetics independent of weight loss.
- It leads to improved glycemic management due to : increased
responsiveness to insulin and so delay the progression of impaired
glucose tolerance to overt diabetes.
- These beneficial effects are directly due to exercise.
- Unfortunately, in one study, only 50% of patients with type 2 diabetes
were able to maintain a regular exercise regimen.

تم بحمدالله
دعواتكم 🩵🩵
عمر- 😇

اللَّهُم نصرك الذى وعدت
اللَّهُم نصرك الذى وعدت
اللَّهُم نصرك الذى وعدت
اللَّهُم غـــــــــــــــزة