Diabetes Mellitus: Comprehensive Overview

1 Definition

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia due to defects in insulin secretion, insulin action, or both. It includes type 1 diabetes (T1DM), type 2 diabetes (T2DM), gestational diabetes, and other specific types, leading to complications affecting multiple organ systems.

2 Etiopathogenesis

Diabetes results from genetic, environmental, and immunological factors:

- **Type 1 Diabetes (T1DM)**:
  - **Autoimmune Destruction**: T-cell-mediated destruction of pancreatic beta cells, often triggered by viral infections or genetic predisposition (HLA-DR/DQ genes).
  - **Risk Factors**: Family history, autoimmune conditions (e.g., thyroiditis), and environmental triggers (e.g., coxsackievirus).
- **Type 2 Diabetes (T2DM)**:
  - **Insulin Resistance**: Impaired insulin signaling in peripheral tissues (e.g., liver, muscle, adipose tissue).
  - **Beta-Cell Dysfunction**: Progressive decline in insulin secretion.
  - **Risk Factors**: Obesity, sedentary lifestyle, genetic predisposition (e.g., TCF7L2 gene), and metabolic syndrome.
- **Gestational Diabetes (GDM)**: Glucose intolerance during pregnancy due to placental hormones causing insulin resistance.
- **Other Types**: Monogenic diabetes (e.g., MODY), secondary diabetes (e.g., pancreatitis, corticosteroid use).

3 Clinical Manifestations

Diabetes presents with acute and chronic manifestations:

- **Acute**: Polyuria, polydipsia, polyphagia, weight loss (especially in T1DM), fatigue, and diabetic ketoacidosis (DKA) in T1DM or hyperosmolar hyperglycemic state (HHS) in

T2DM.

- **Chronic Complications**:
  - **Microvascular**: Retinopathy, nephropathy, neuropathy.
  - **Macrovascular**: Coronary artery disease, stroke, peripheral artery disease.
  - **Other**: Increased infection risk, delayed wound healing.

4 Pathophysiology

The pathophysiology of diabetes involves impaired insulin function leading to hyperglycemia and complications. The flowchart below illustrates the key mechanisms for T1DM and T2DM.

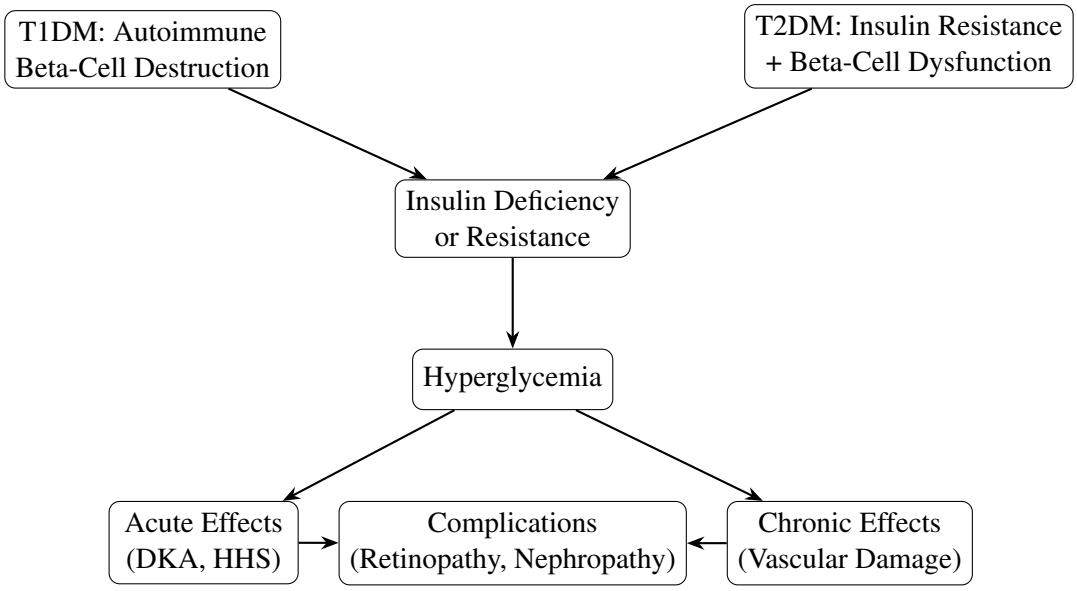

Figure 1: Pathophysiology of Diabetes Mellitus

5 Symptoms

- **Common Symptoms**:
  - Polyuria (frequent urination due to osmotic diuresis).
  - Polydipsia (excessive thirst).
  - Polyphagia (increased hunger, especially in T1DM).
  - Unexplained weight loss (more common in T1DM).
  - Fatigue and weakness.
- **Severe Cases**:
  - DKA (T1DM): Nausea, vomiting, abdominal pain, fruity breath, confusion.
  - HHS (T2DM): Severe dehydration, confusion, seizures.

  - Neuropathy symptoms: Numbness, tingling in extremities.

6 Diagnosis

Diagnosis is based on glycemic criteria and clinical evaluation:

- **Glycemic Criteria (ADA/WHO)**:
  - Fasting plasma glucose (FPG) $\geq$126 mg/dL (7.0 mmol/L).
  - 2-hour plasma glucose $\geq$200 mg/dL (11.1 mmol/L) during oral glucose tolerance test (OGTT).
  - HbA1c $\geq$6.5%.
  - Random plasma glucose $\geq$200 mg/dL with symptoms.
- **Clinical Evaluation**: Assess symptoms, family history, and risk factors (e.g., obesity, gestational diabetes).
- **Additional Tests**: C-peptide or autoantibodies (e.g., anti-GAD) to differentiate T1DM from T2DM; urine albumin for nephropathy screening.
- **Screening**: Regular screening for at-risk individuals (e.g., age >45, BMI >25 kg/m^2, family history).

7 Nonpharmacological Management

Lifestyle modifications are critical for diabetes management:

- **Dietary Management**:
  - Follow a balanced diet with controlled carbohydrates (e.g., low glycemic index foods).
  - Increase fiber intake (e.g., whole grains, vegetables).
  - Limit refined sugars and saturated fats.
- **Physical Activity**: 150–300 minutes/week of moderate aerobic exercise (e.g., brisk walking) plus resistance training to improve insulin sensitivity.
- **Weight Management**: Achieve and maintain BMI of 18.5–24.9 kg/m^2; 5–10% weight loss for T2DM.
- **Blood Glucose Monitoring**: Regular self-monitoring (e.g., glucometer) or continuous glucose monitoring (CGM) for T1DM and insulin-treated T2DM.
- **Patient Education**: Teach carbohydrate counting, hypoglycemia management, and foot care.
- **Smoking Cessation**: Eliminate smoking to reduce cardiovascular risk.
- **Psychosocial Support**: Address stress and mental health through counseling or support groups.

8 Pharmacological Management

Medications aim to achieve glycemic control and prevent complications:

- **Type 1 Diabetes**:
  - **Insulin Therapy**: Lifelong insulin replacement (basal-bolus regimen or insulin pump).
    - Basal: E.g., insulin glargine (10–20 units/day, adjusted).
    - Bolus: E.g., insulin aspart or lispro with meals.
  - **Adjunctive Therapy**: Pramlintide (amylin analog) to reduce postprandial glucose.
- **Type 2 Diabetes**:
  - **Metformin**: First-line (500–2000 mg/day) to reduce hepatic glucose production.
  - **Sulfonylureas**: E.g., glimepiride (1–8 mg/day) to stimulate insulin secretion.
  - **DPP-4 Inhibitors**: E.g., sitagliptin (100 mg/day) to enhance incretin effects.
  - **SGLT2 Inhibitors**: E.g., empagliflozin (10–25 mg/day) to increase glucose excretion.
  - **(**GLP-1 Receptor Agonists: E.g., liraglutide (0.6–1.8 mg/day) to enhance insulin secretion and promote weight loss.
  - **Thiazolidinediones**: E.g., pioglitazone (15–45 mg/day) to improve insulin sensitivity.
  - **Insulin**: Added for advanced T2DM (e.g., basal insulin like glargine).
- **Gestational Diabetes**: Insulin preferred; metformin or glyburide in select cases.
- **Complication Management**: ACE inhibitors for nephropathy, statins for dyslipidemia, aspirin for cardiovascular risk.
- **Stepwise Approach**: Start with metformin (T2DM), add agents based on HbA1c goals (<7% for most) and patient factors.