Type 2 Diabetes: Clinical Breakdown

Pathophysiology, Insulin Resistance, Diagnostic Criteria, Microvascular/Macrovascular Complications, and Management Principles

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by peripheral insulin resistance paired with progressive secretory dysfunction of pancreatic beta cells. Over time, impaired insulin action leads to chronic hyperglycemia, which drives microvascular and macrovascular damage across multiple organ systems.

> **Core Clinical Principle:** Type 2 diabetes stems from a dual defect: target tissues (skeletal muscle, liver, adipose tissue) fail to respond effectively to normal insulin levels, and pancreatic beta cells ultimately fail to compensate by producing adequate insulin.

1. Diagnostic Criteria & Glycemic Thresholds

Standardized clinical diagnostics rely on blood glucose and glycated hemoglobin metrics.

Diagnostic Test	Prediabetes Range	Diabetes Threshold
Glycated Hemoglobin (HbA1c)	5.7% – 6.4%	6.5% or higher
Fasting Plasma Glucose (FPG)	100 – 125 mg/dL	126 mg/dL or higher
Oral Glucose Tolerance Test (OGTT)	140 – 199 mg/dL (2-hour)	200 mg/dL or higher
Random Plasma Glucose	—	200 mg/dL + classic symptoms

2. Pathophysiology & Metabolic Progression

The progression of T2DM involves interrelated metabolic abnormalities that compound over time.

- **Insulin Resistance:** Receptors on muscle and liver cells exhibit decreased sensitivity to insulin, impairing glucose uptake and suppression of hepatic gluconeogenesis.
- **Beta-Cell Exhaustion:** Initially, pancreatic beta cells secrete higher insulin levels to overcome resistance (hyperinsulinemia). Over time, glucotoxicity, lipotoxicity, and amyloid deposition lead to beta-cell apoptosis and relative insulin deficiency.
- **Incretin Dysfunction & Glucagon Dysregulation:** Decreased GLP-1 and GIP incretin effects impair postprandial insulin release, while alpha cells continue inappropriate glucagon secretion, exacerbating hyperglycemia.

3. Complications & Comprehensive Management

Chronic hyperglycemia damages blood vessels throughout the body, resulting in systemic complications.

- **Microvascular & Macrovascular Complications:** Affects microcirculation (causing diabetic retinopathy, nephropathy, and peripheral neuropathy) and macrocirculation (accelerating atherosclerosis, coronary artery disease, stroke, and peripheral artery disease).
- **Multidisciplinary Management:** Combines medical nutrition therapy, structured physical activity, self-monitoring of blood glucose, and targeted pharmacotherapy (metformin, SGLT2 inhibitors, GLP-1 receptor agonists, sulfonylureas, or insulin) tailored to glycemic goals.