inical Reference: Diabetes Mellitus Type 2 - Diagnosis and Manageme

1. Epidemiology and Pathophysiology

Type 2 diabetes mellitus (T2DM) affects over 37 million Americans and accounts for 90-95% of all diabetes cases. The disease is characterized by progressive insulin resistance and relative insulin deficiency due to beta-cell dysfunction. Major risk factors include obesity (BMI >= 25), family history, physical inactivity, history of gestational diabetes, polycystic ovary syndrome, and certain ethnicities (African American, Hispanic, Native American, Asian American). Complications include cardiovascular disease, nephropathy, retinopathy, neuropathy, and increased infection risk.

2. Diagnostic Criteria

Diagnosis requires one of the following confirmed on two separate occasions unless unequivocal hyperglycemia is present: Fasting plasma glucose (FPG) of 126 mg/dL or higher. Oral glucose tolerance test (OGTT) 2-hour value of 200 mg/dL or higher. Hemoglobin A1c of 6.5% or higher using a NGSP-certified method. Random plasma glucose of 200 mg/dL or higher with classic symptoms (polyuria, polydipsia, unexplained weight loss). Prediabetes: FPG 100-125 mg/dL, OGTT 140-199 mg/dL, or A1c 5.7-6.4%.

3. Glycemic Targets

Standard A1c target: less than 7.0% for most non-pregnant adults. This has been shown to reduce microvascular complications. More stringent target (A1c < 6.5%): consider for patients with short disease duration, long life expectancy, and no significant cardiovascular disease, if achievable without significant hypoglycemia. Less stringent target (A1c < 8.0%): consider for patients with history of severe hypoglycemia, limited life expectancy, advanced complications, extensive comorbidities, or long-standing diabetes. Fasting glucose target: 80-130 mg/dL. Post-prandial glucose target: less than 180 mg/dL (measured 1-2 hours after meal).

4. First-Line Therapy - Metformin

Metformin is the preferred initial pharmacologic agent for T2DM. Starting dose: 500mg once daily with the evening meal, titrate by 500mg weekly to target dose of 1000mg twice daily. Maximum dose: 2550mg daily in divided doses. Mechanism: reduces hepatic glucose production, improves insulin sensitivity, modestly reduces weight. Contraindications: eGFR below 30 mL/min (do not initiate), eGFR 30-45 (reduce dose to 1000mg daily, monitor renal function every 3 months). Common side effects: gastrointestinal (nausea, diarrhea, abdominal discomfort) - usually self-limited with dose titration. Extended-release formulation may improve GI tolerability. Monitor vitamin B12 levels annually.

5. Second-Line and Add-On Therapies

If A1c remains above target after 3 months of metformin at maximum tolerated dose, add a second agent based on patient factors: SGLT2 inhibitors (empagliflozin 10-25mg, dapagliflozin 5-10mg) - preferred for patients with established cardiovascular disease, heart failure, or CKD. Provide cardiovascular and renal

protection independent of glucose lowering. GLP-1 receptor agonists (semaglutide 0.25-1mg weekly, liraglutide 0.6-1.8mg daily, dulaglutide 0.75-4.5mg weekly) - preferred for patients needing significant A1c reduction or weight loss. DPP-4 inhibitors (sitagliptin 100mg daily) - well tolerated, weight neutral, but less potent. Sulfonylureas (glimepiride 1-4mg daily, glipizide 5-20mg daily) - effective and low cost, but risk of hypoglycemia and weight gain. Insulin: consider early if A1c above 10%, symptomatic hyperglycemia, or evidence of catabolism.

6. Insulin Therapy

Basal insulin initiation: start with 10 units or 0.1-0.2 units/kg daily of insulin glargine, detemir, or degludec. Titrate by 2-4 units every 3 days to achieve fasting glucose target of 80-130 mg/dL. If A1c remains above target on basal insulin with fasting glucose at target, add prandial insulin: rapid-acting insulin (lispro, aspart, or glulisine) 4 units or 10% of basal dose before the largest meal. Adjust by 1-2 units every 3 days based on post-prandial glucose. Educate patients on injection technique, hypoglycemia recognition and treatment (15g fast-acting carbohydrate rule), sick day management, and blood glucose monitoring frequency (minimum fasting daily, pre-prandial if on prandial insulin).

7. Complication Screening Schedule

Annual screening requirements for all T2DM patients: dilated eye exam by ophthalmologist (retinopathy screening), foot exam with monofilament testing and pedal pulse assessment (neuropathy and peripheral vascular disease), urine albumin-to-creatinine ratio and eGFR (nephropathy), lipid panel, comprehensive metabolic panel. Every visit: blood pressure measurement (target < 130/80 mmHg), weight and BMI, medication adherence and side effect review, hypoglycemia assessment. A1c measurement every 3 months if not at target, every 6 months if stable and at target.

8. Cardiovascular Risk Reduction

Diabetes is a cardiovascular disease equivalent. All T2DM patients require aggressive cardiovascular risk management: statin therapy for all patients aged 40-75 (moderate intensity: atorvastatin 10-20mg or rosuvastatin 5-10mg; high intensity for those with ASCVD or 10-year risk > 20%: atorvastatin 40-80mg or rosuvastatin 20-40mg). Aspirin 75-162mg daily for secondary prevention in patients with established ASCVD. For primary prevention, aspirin may be considered in patients with high cardiovascular risk after discussing bleeding risk. Blood pressure target: less than 130/80 mmHg. Smoking cessation counseling at every visit with pharmacotherapy (varenicline, bupropion, or nicotine replacement) offered to all current smokers.