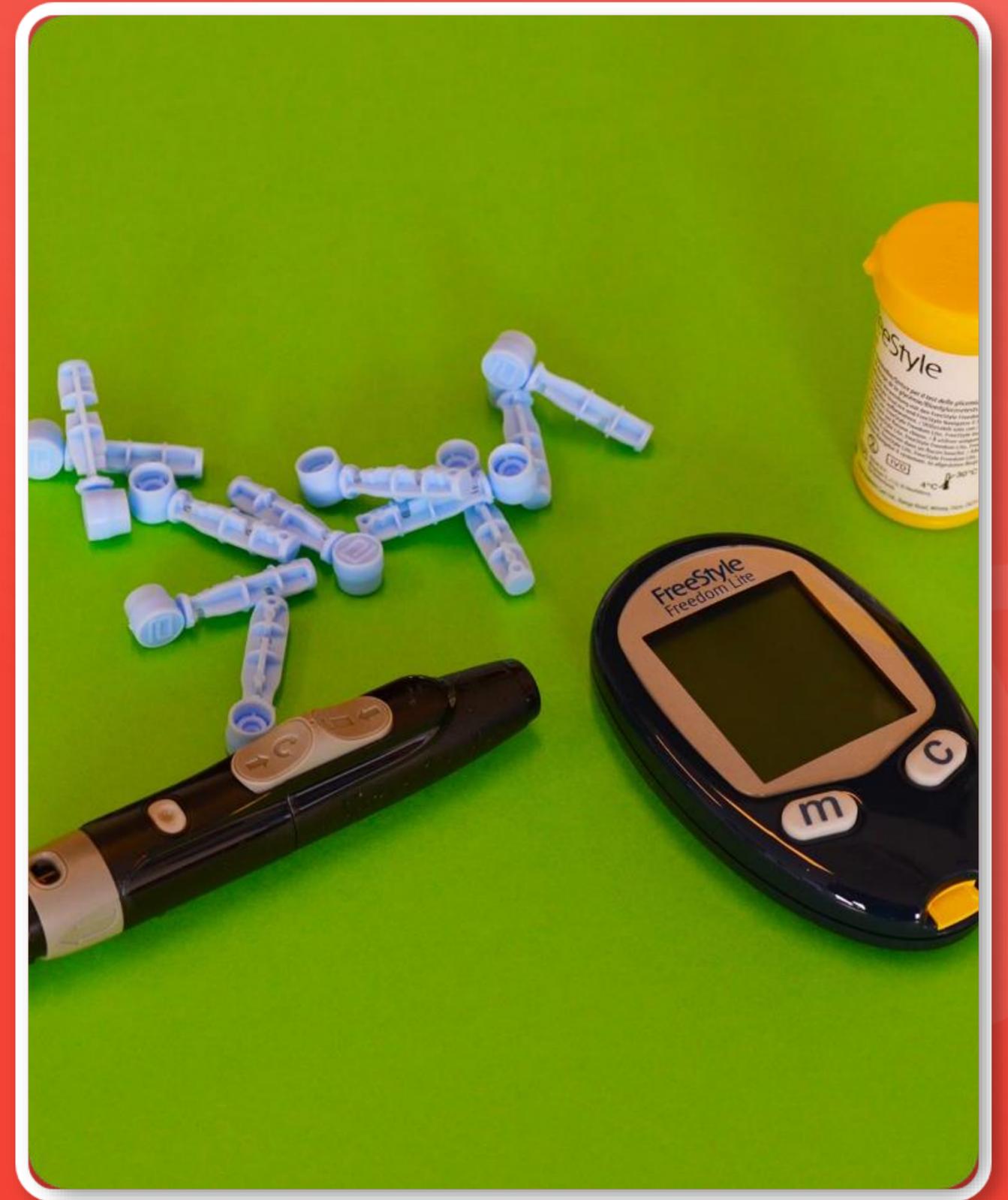
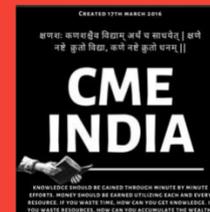


Type 5 Diabetes: Malnutrition-Related Diabetes

New Classification by IDF

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Introduction and Background



- 1 Definition: Type 5 diabetes is a newly recognized form of diabetes caused by chronic malnutrition.
- 2 Recognition: The IDF officially endorsed Type 5 at the World Diabetes Congress (Bangkok, April 2025).
- 3 History: Though noted over 70 years ago, Type 5 was long overlooked.
- 4 Distinctiveness: Unlike Type 1 and Type 2, Type 5 arises from impaired pancreatic development due to early-life undernutrition.

Epidemiology and Demographics



An estimated 20–25 million people have Type 5 diabetes worldwide.



Most patients are lean adolescents or young adults from poor households.



Type 5 has been historically underdiagnosed and misclassified as Type 1 or Type 2.



There are no well-defined genetic risk factors; environmental (nutritional) factors dominate.



It predominantly affects low- and middle-income countries, especially Asia and Africa.



Body mass index (BMI) is typically very low (often <18.5 – 19 kg/m²).



Onset is usually in the teens or 20s, with a male predominance noted in some reports.

Pathophysiology and Mechanisms

Chronic protein-energy malnutrition during critical growth periods leads to underdevelopment of the pancreas and pancreatic islets.

- 1 This results in severely reduced β -cell mass and insulin secretion capacity.

Type 5 is characterized by severe insulin deficiency.

- 2 Recent studies show a 'profound defect' in β -cell secretion of insulin, not insulin resistance.

Patients generally lack islet autoantibodies (GAD65, IA-2, ZnT8).

- 3 They do not have significant insulin resistance, with normal or increased insulin sensitivity due to leanness.

Patients exhibit extreme hyperglycemia with relatively low endogenous insulin.

- 4 They require high doses of exogenous insulin for glycemic control, yet remain hyperglycemic.

There is no single gene mutation known to cause Type 5.

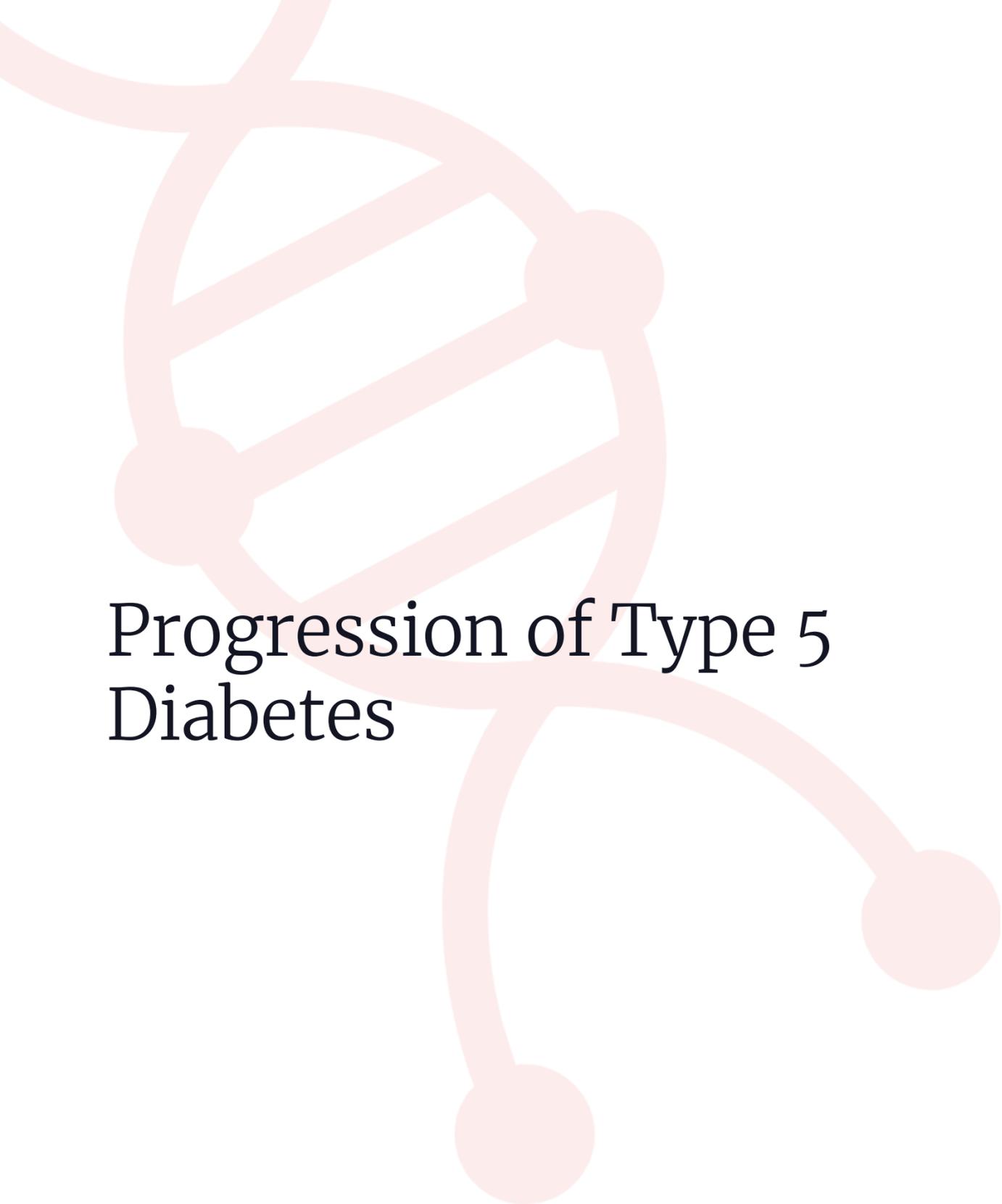
- 5 The condition likely involves developmental/epigenetic changes in β -cell gene expression triggered by undernutrition.

Historically, the WHO term 'malnutrition-related diabetes mellitus (MRDM)' included two forms: protein-deficient pancreatic diabetes (PDPD) and fibrocalculous pancreatic diabetes (FCPD).

- 6 These now fall under the umbrella of Type 5.

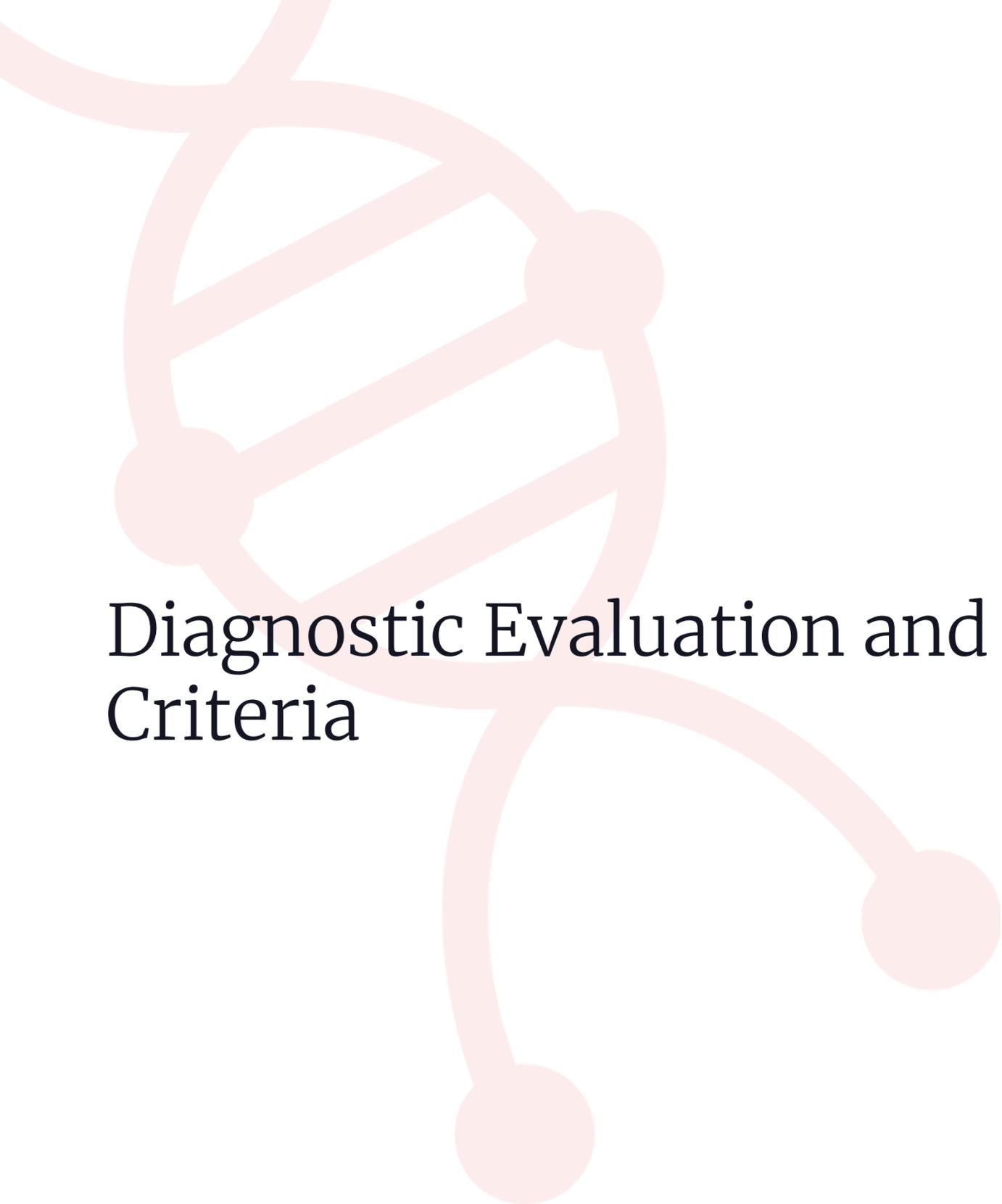
Clinical Features and Presentation

- 1 Typically adolescent or young adult onset (teens to 30s) with acute or insidious hyperglycemia
- 2 Patients are chronically undernourished, often stunted with low muscle and fat mass
- 3 Classic symptoms include polyuria, polydipsia, polyphagia, and severe weight loss
- 4 Extreme fatigue and generalized weakness are common
- 5 Frequent infections occur, likely due to protein deficiency
- 6 Very low BMI (<18.5), muscle wasting, cachexia observed
- 7 Marked hyperglycemia with fasting glucose often above 200 mg/dL
- 8 Ketoacidosis is uncommon; patients maintain low insulin to prevent ketosis
- 9 Low C-peptide levels relative to blood glucose, reflecting low endogenous insulin
- 10 Autoantibodies (GAD, IA-2, IAA) are typically negative



Progression of Type 5 Diabetes

- 1 Type 5 tends to progress rapidly if untreated: β -cell function deteriorates further.
- 2 Early reports suggest high early mortality if not properly managed.
- 3 Research leads to designation of new type of diabetes: Type 5.
- 4 For survivors, chronic complications (retinopathy, neuropathy, nephropathy) are expected as in other insulin-dependent diabetes.
- 5 Data are limited regarding the long-term effects of Type 5 Diabetes.



Diagnostic Evaluation and Criteria

- 1 Clinical Suspicion: Diagnose Type 5 in any lean, malnourished young person with diabetes who lacks classic Type 1/2 features. Key red flags: history of childhood undernutrition, BMI <18.5, and needing large insulin doses with persistent hyperglycemia.
- 2 Exclusion of Other Types: Testing should first rule out other causes: measure islet autoantibodies (should be negative), evaluate for insulin resistance, and assess family history for monogenic diabetes.
- 3 Laboratory Tests: Confirm persistent hyperglycemia (fasting plasma glucose, OGTT, A1c). Check C-peptide (low or inappropriately normal) and screen for pancreatic exocrine disease.
- 4 Nutritional Assessment: Document anthropometrics (height, weight, BMI) and evidence of stunting or wasting. Check laboratory nutritional markers (albumin, prealbumin, micronutrient levels).
- 5 No Formal Criteria (Yet): There are no validated diagnostic criteria as of 2025. Diagnosis is clinical, of exclusion.

Differential Diagnosis

- 1 Type 1 Diabetes: Unlike Type 1, Type 5 patients lack autoimmune markers. Both can present in youth and with high glucose, but Type 1 often presents with ketoacidosis and requires insulin promptly. Type 5 often presents without ketosis and paradoxically does not improve with insulin alone.
- 2 Type 2 Diabetes: Type 2 occurs in overweight/obese adults with insulin resistance. In contrast, Type 5 patients are lean, undernourished, and insulin-sensitive. The metabolic syndrome is absent in Type 5.
- 3 Latent Autoimmune Diabetes in Adults (LADA): LADA is adult-onset autoimmune diabetes with slow progression to insulin dependence. Type 5 patients do not have autoantibodies and typically present at a younger age.
- 4 MODY (Monogenic Diabetes): Classic MODY involves a dominant gene mutation with strong family history and often kidney/pancreas anomalies. Type 5 is non-familial, due to malnutrition, and patients usually lack the characteristic gene defects of MODY.
- 5 Ketosis-Prone (Type A) Diabetes (KPD): KPD often affects people of African or Hispanic descent who present with DKA but may later come off insulin. KPD patients are usually overweight. In Type 5, DKA is rare and insulin needs persist.
- 6 Fibrocalculous Pancreatic Diabetes (FCPD): A tropical pancreatitis form with pancreatic calcification and secondary diabetes. If imaging shows pancreatic stones or calcifications, FCPD may be diagnosed. Most Type 5 patients do not have evident calcifications on imaging.
- 7 Other secondary causes: Rule out endocrine/exocrine causes (Cushing's, acromegaly, hemochromatosis). Type 5 is differentiated by the strong context of malnutrition and absence of other organ disorders.

Management Strategies

- 1 No Established Guidelines Yet: As of 2025, there are no official treatment guidelines specifically for Type 5.
- 2 Nutritional Rehabilitation: The cornerstone of management is aggressive nutritional support. Provide adequate calories and high-protein diet to reverse malnutrition.
- 3 Glycemic Control – Medication: Patients are insulin-deficient but may manage with oral agents more than with high-dose insulin.
- 4 Insulin Therapy: If oral agents are insufficient, insulin is used carefully in small increments to prevent hypoglycemia.
- 5 Monitoring and Targets: Regular glucose monitoring is essential. Aim for individualized glycemic targets.
- 6 Adjunctive Care: Encourage moderate physical activity and immunize against infections as patients are prone to infections.
- 7 Health System Implications: In low-resource settings, oral drugs are cost-effective. Engage community health workers to identify cases.

Prognosis and Follow-Up

- 1 High Early Mortality: Historically, prognosis was very poor without targeted treatment: many patients died within a year of diagnosis.
- 2 Main causes were complications of diabetes combined with malnutrition (infections, organ failure).
- 3 Chronic Complications: Survivors develop typical insulin-deficiency complications.
- 4 Risks of retinopathy, nephropathy, neuropathy exist if hyperglycemia persists.
- 5 However, macrovascular disease (heart attacks, strokes) might be less frequent given low cholesterol and absence of atherosclerotic risk factors, though data are lacking.
- 6 Effect of Treatment: With proper nutrition and glucose control, many patients can stabilize.
- 7 Anecdotal reports suggest weight gain and better glycemic indices on a high-protein diet and oral meds.
- 8 Follow-Up: These patients need intensive follow-up.
- 9 Multidisciplinary care (endocrinology, nutritionist, social services) yields best outcomes.
- 10 Research Gaps: Longitudinal data are limited. Ongoing studies and registries (in development) will clarify long-term outcomes.

Summary and Clinical Pearls

- 1 Type 5 Diabetes = Malnutrition-Related DM: New IDF classification (2025) for severe insulin-deficient diabetes caused by chronic undernutrition
- 2 Epidemiology: 20–25 million affected, mainly lean adolescents/young adults in Asia/Africa
- 3 Often > TB or on par with HIV prevalence in endemic areas
- 4 Chronic protein-energy malnutrition → impaired pancreatic β -cell development → profound insulinopenia
- 5 No autoimmunity or insulin resistance
- 6 Clinical Clues: Extremely low BMI (<18.5), history of childhood malnutrition, high blood sugars without ketosis
- 7 Frequent infections and muscle wasting
- 8 Negative islet autoantibodies, low C-peptide relative to glucose, normal insulin sensitivity
- 9 Exclusion diagnosis of Type 1/2, LADA, MODY
- 10 Utilize history of malnutrition and absence of obesity

Future Outlook and Take-Home Points

- 1 Clinicians should think Type 5 when encountering thin diabetic patients from poor backgrounds.
- 2 Screen at-risk youth in LMICs for undiagnosed diabetes (e.g., during malnutrition or TB clinics).
- 3 The IDF working group (Hawkins et al.) will publish formal diagnostic criteria and treatment guidelines in the next 1–2 years.
- 4 Ongoing studies (e.g., Diabetes Care 2022) are clarifying metabolic defects.
- 5 Recognizing Type 5 improves equity by addressing a long-neglected population.
- 6 Integrate Type 5 diabetes into national diabetes strategies, nutrition programs, and global burden estimates.
- 7 No ketosis despite high glucose is a hallmark.
- 8 Avoid overtreating with insulin (risk of hypoglycemia).
- 9 Instead, improve nutrition and consider oral secretagogues first.
- 10 Needed on genetic/epigenetic markers, optimal drug regimens, and long-term outcomes.



Thanks