Diabetes mellitus

Diabetes mellitus is characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action or both

Classification of diabetes mellitus

- **Type 1 diabetes** :Type 1 diabetes is characterized by destruction of the pancreatic beta cells, leading to absolute insulin deficiency

- This is usually due to autoimmune destruction of the beta cells (type 1A)
- Some patients with absolute insulin deficiency have no evidence of autoimmunity and have no other known cause for beta cell destruction(idiopathic or type 1B diabetes mellitus)

❑**TYPE 2 DIABETES**: Type 2 diabetes is by far the most common type of diabetes in adults and is characterized by hyperglycemia and variable degrees of insulin deficiency and resistance

❑**Monogenic diabetes:**

- *Maturity onset diabetes of the young* — Maturity onset diabetes of the young (MODY) is a clinically heterogeneous disorder characterized by noninsulin-dependent diabetes diagnosed at a young age (<25 years) with autosomal dominant transmission and lack of autoantibodies

- *Genetic defects in mitochondrial DNA* — Maternally inherited diabetes and deafness (MIDD) is a rare mitochondrial disorder

  Other abnormalities seen include cardiac conduction defects, gestational diabetes, proteinuria, and neuropathy

- *Wolfram syndrome* —Wolfram or DIDMOAD (diabetes insipidus, diabetes mellitus, optic atrophy, and deafness) syndrome

- *Genetic defects in insulin action* – Leprechaunism,Rabsonmendenhall syndrome, Lipoatrophic diabetes

- *Diseases of the exocrine system* – Cystic fibrosis, hereditary hemochromatosis, and chronic pancreatitis

- *Endocrine abnormalities*– Cushing syndrome, growth-hormone excess, glucagon-secreting tumors, catecholamine excess in pheochromocytoma

- *Drug-induced diabetes* – A number of drugs (eg, glucocorticoids, HIV protease inhibitors, cyclosporine, L-asparaginase, and tacrolimus) and atypical antipsychotic agents can impair glucose tolerance by inhibiting insulin secretion, increasing hepatic glucose production, or causing insulin resistance

- *Gestational Diabetes*

Type 1 diabetes mellitus (T1DM)

- common chronic diseases in childhood
- T1DM remains the most common form of diabetes in childhood

- It most commonly presents in childhood, but one-fourth of cases are diagnosed in adults.

RISK FACTORS

Both genetic and environmental factors contribute to the risk of developing T1DM

Genetic susceptibility: Polymorphisms of multiple genes are reported to influence the risk of type 1A diabetes, including genes in both the major histocompatibility complex (MHC) and elsewhere in the genome, but only human leukocyte antigen (HLA) alleles have a large effect, in particular,DR3 and DR4

The lifetime risk of developing T1DM is significantly increased in close relatives of a patient with T1DM:

- No family history – 0.4 percent
- Offspring of an affected mother – 1 to 4 percent
- Offspring of an affected father – 3 to 8 percent
- Offspring with both parents affected – Reported as high as 30 percent
- Non-twin sibling of affected patient – 3 to 6 percent by age 20 years and 10 percent by 60 years
- Dizygotic twin – 8 percent
- Monozygotic twin – 30 percent within 10 years of diagnosis of the first twin and 65 percent concordance by age 60 years

Triggering factors:

- Viral infections
- Diet
- Higher socioeconomic status
- Obesity
- Vitamin D deficiency
- Perinatal factors such as maternal age, history of preeclampsia, and neonatal jaundice
- Low birth weight decreases the risk of developing T1DM, while high birth weight for gestational age and lower gestational age at birth may increase the risk for T1DM

Diagnostic criteria for diabetes

- Diabetes mellitus is diagnosed based upon one of the following four signs of abnormal glucose metabolism :

1. Fasting plasma glucose ≥126 mg/dL (7 mmol/L) on more than one occasion
2. Random venous plasma glucose ≥200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycemia
3. Plasma glucose ≥200 mg/dL (11.1 mmol/L) measured two hours after a glucose load of 1.75 g/kg (maximum dose of 75 g) in an oral glucose tolerance test
4. Glycated hemoglobin (A1C) ≥6.5 percent

Type 1 versus type 2 diabetes

Clinical characteristics:

●*Body habitus* – Patients with T2DM are usually obese (body mass index ≥95th percentile for age and gender). In contrast, children with T1DM are usually not obese and often have a recent history of weight loss, although up to 25 percent are overweight (body mass index ≥85th to 95th percentile)

●*Age* – Patients with T2DM generally present after the onset of puberty, whereas those with T1DM often present at an earlier age. Approximately 45 percent of children with T1DM present before 10 years of age . By contrast, almost all cases of T2DM present after 10 years of age

- *Insulin resistance* – Patients with T2DM frequently have acanthosis nigricans (a sign of insulin resistance), hypertension, dyslipidemia, and polycystic ovary syndrome (in girls). These findings are less likely in children with T1DM

- *Family history* – Up to 10 percent of patients with T1DM have an affected close relative, whereas 75 to 90 percent of those with T2DM have an affected close relative

Laboratory :

●*Antibodies* –T1DM is suggested by the presence of antibodies to glutamic acid decarboxylase (GAD), islet cell, insulin, the tyrosine phosphatases (insulinoma-associated protein 2 [IA-2] and IA-2 beta), and zinc transporter (ZnT8)

If one or more of the antibodies is present, and especially if two or more are positive, the patient should be presumed to have type 1 diabetes

However, the absence of pancreatic autoantibodies does not rule out the possibility of T1DM

●*Insulin and C-peptide levels* – High fasting insulin and C-peptide levels suggest T2DM. Levels are inappropriately low or in the normal range relative to the concomitant plasma glucose concentration in T1DM

At presentation, insulin and C-peptide levels may be suppressed by severe hyperglycemia and illness

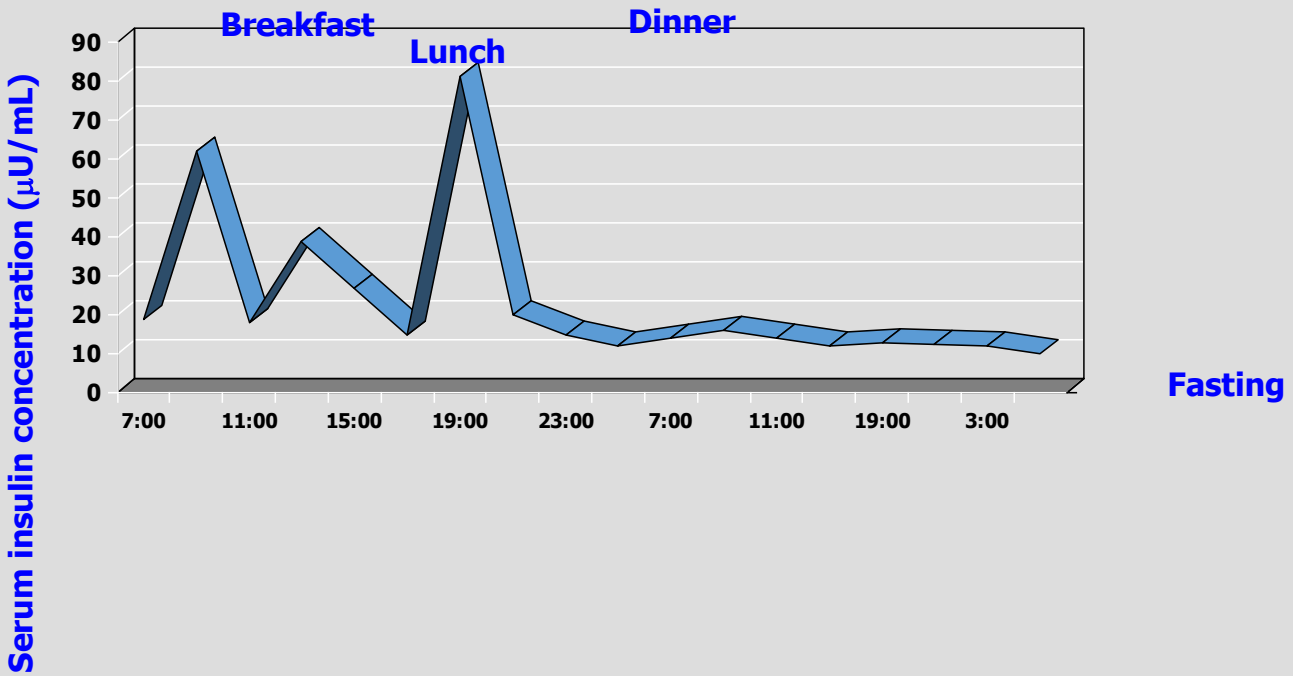
It is usually best to assess these levels after the newly diagnosed patient has recovered from acute illness

management of type 1 diabetes

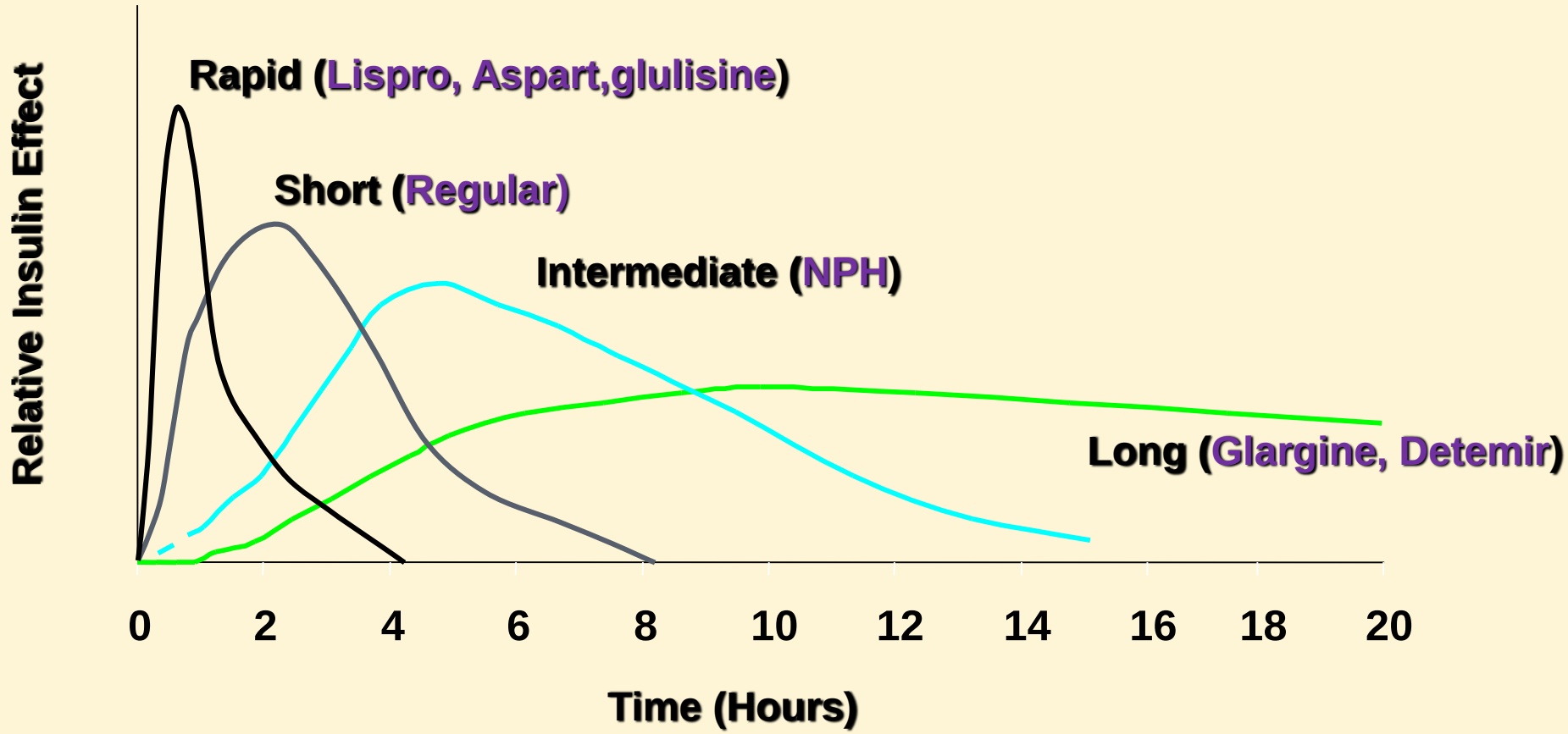
The management of T1DM may be divided into three phases:

- Ketoacidosis
- Transitional period
- Continuing phase of guidance of the diabetic child and his or her family for daily living ,integrating insulin regimens, nutritional intake, exercise and glucose monitoring to achieve as near normal glucose conttrol

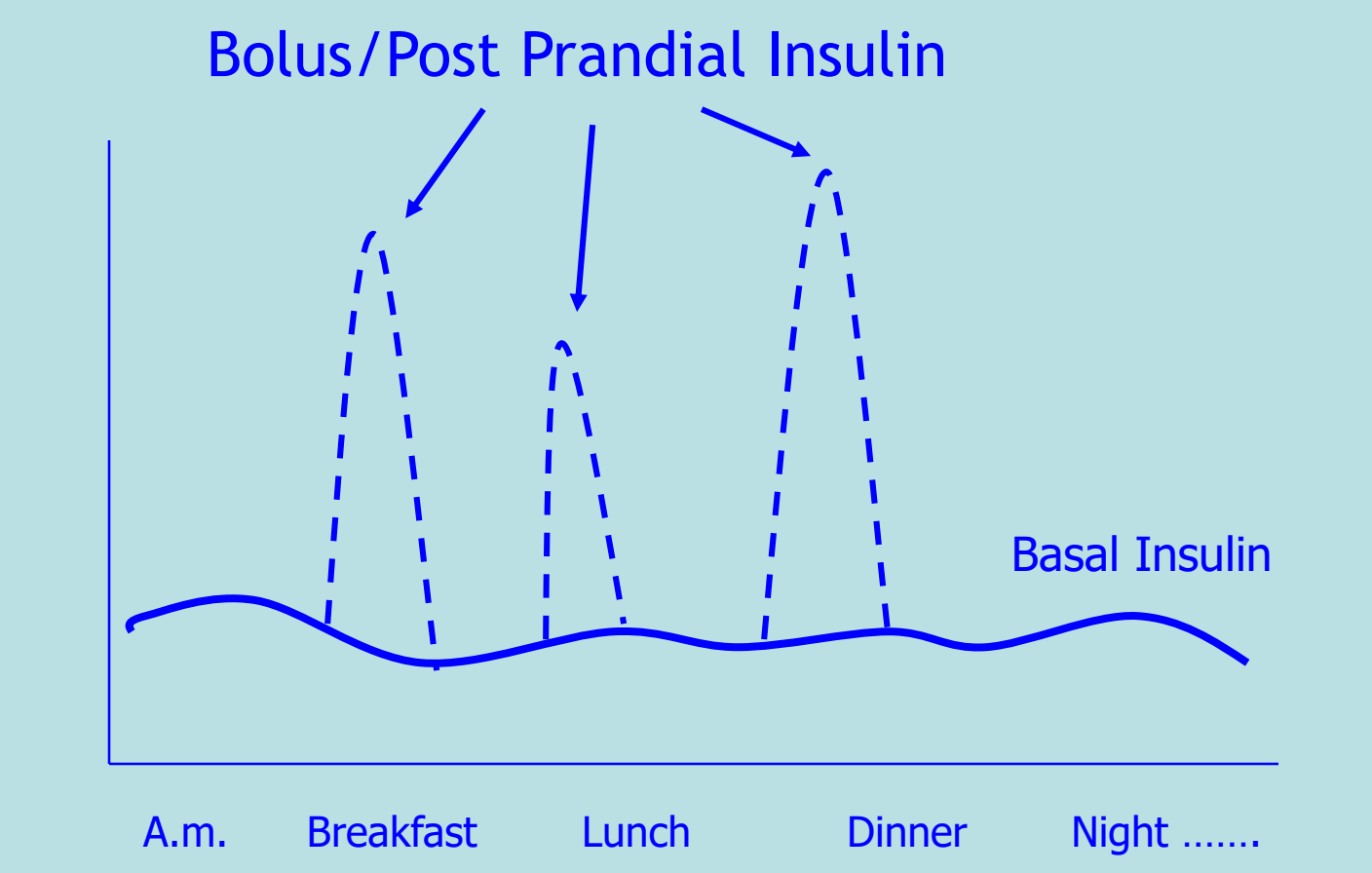
Normal Endogenous Insulin Secretion



Insulin Time Action Curves



To mimic physiological conditions



multiple injections

- rapid-acting insulin given with meals in combination with long-acting basal insulin given at bedtime or morning

- This regimen provides flexibility but requires administration of many injections per day

- After the total daily dose of insulin is determined, 30% to 50% are given as long-acting insulin, and the remainder is given as fast-acting insulin ,as carbohydrate dosing

- fixed mixed split dosing regimen
- Insulin pump