DIABETES MELLITUS

INTRODUCTION

- DM is a chronic disorder of carbohydrate, fat and protein metabolism resulting from insulin deficiency or abnormality in the use of insulin which results in hyperglycemia (increased blood glucose level)

- Insulin is secreted by beta cells of Pancreas
- About 40-50 units of insulin is secreted daily
- Insulin inhibits glucagon activity and allows glucose to move into cells and make energy

Types of D.M

- Type-I Diabetes Mellitus (Also known as Insulin dependent Diabetes Mellitus)
- Type-II Diabetes Mellitus (Also called non insulin dependent diabetes mellitus)

ETIOLOGY

GENETIC FACTORS	ENVIRONMENTAL FACTORS	FACTORS WITHIN INDIVIDUAL
•Genetic mutation of β-cells •Mutation in mitochondrial DNA •Genetic defects in insulin action	• Obesity •Lifestyle changes •Lack of physical activity	TYPE 1 DM •Production of autoantibodies to destroy β- cells •Deficiency in insulin secretion TYPE 2 DM •Insulin resistance

SIGNS AND SYMPTOMS

- Ketoacidosis
- Ketonuria

Ketones are by-products of muscle and fat breakdown when there is no enough insulin

- Glycosuria (presence of glucose in urine)
- Polydypsia (increased thirst)
- Polyuria (increased frequency of urination)
- Polyphagia (extreme hunger)
- Weight loss
- Fatigue and headache
- Blurred vision
- Frequent infections

PATHOPHYSIOLOGY OF TYPE -1 DM

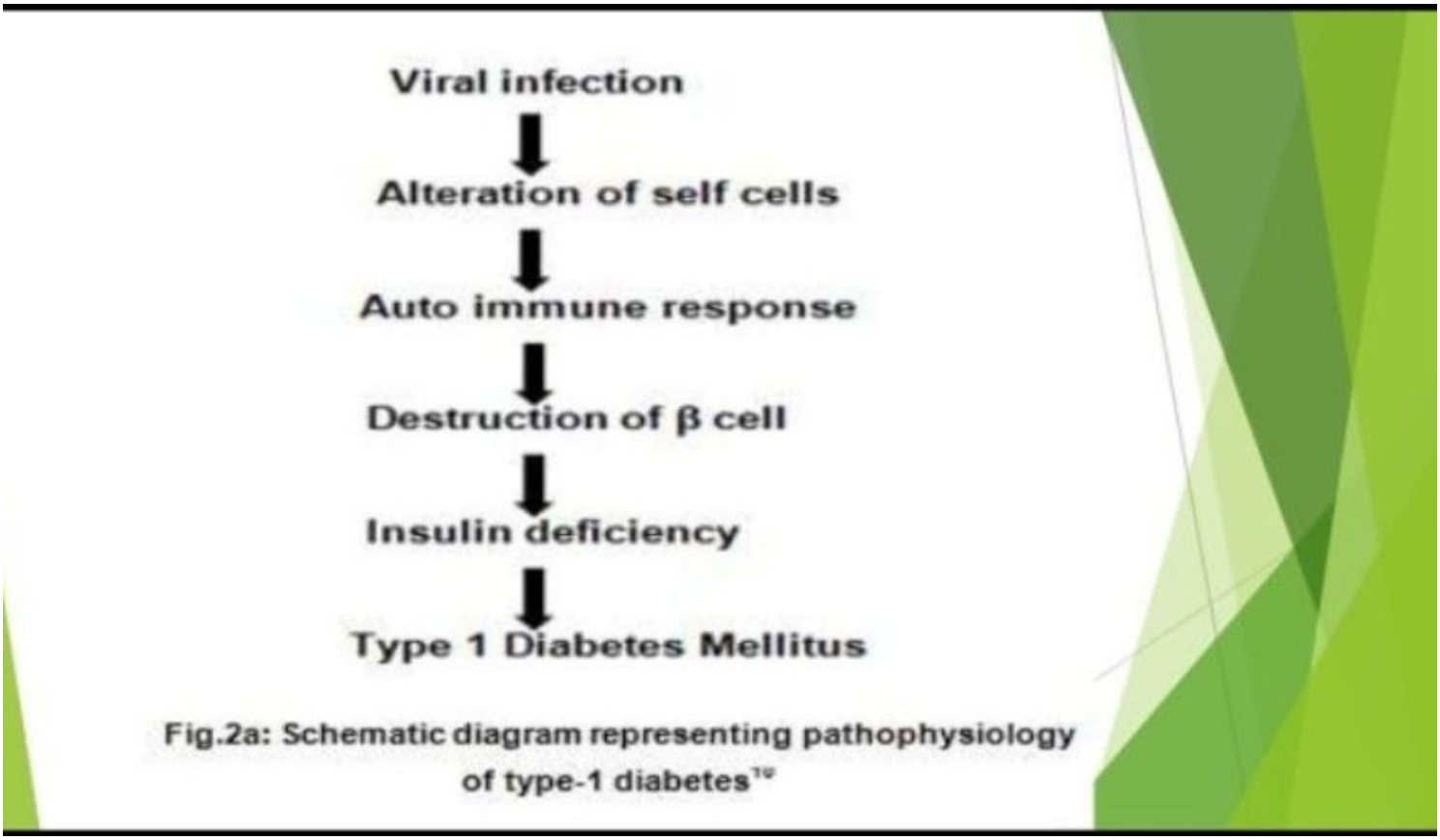
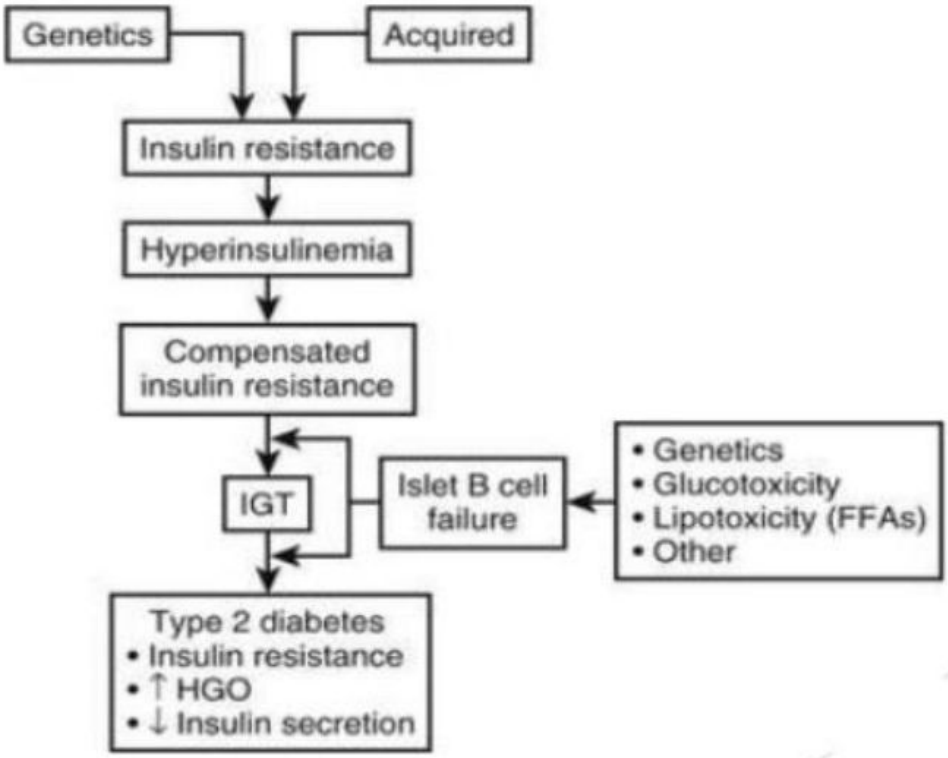


Fig.2a: Schematic diagram representing pathophysiology of type-1 diabetes[19]

- Type 1 Diabetes is characterized by autoimmune destruction of insulin producing cells in the pancreas by CD4+ and CD8+ T cells and macrophages infiltrating the islets
- Approximately 85% of patients have circulating islet cell antibodies, and the majorities also have detectable anti-insulin antibodies before receiving insulin therapy. Most islet cell antibodies are directed against glutamic acid decarboxylase (GAD) within pancreatic B cells

- The autoimmune destruction of pancreatic ß-cells, leads to a deficiency of insulin secretion which results in the metabolic derangements associated with T1DM. In addition to the loss of **insulin** secretion, the function of pancreatic α-cells is also abnormal and there is excessive secretion of glucagon in T1DM patients
- Deficiency in insulin leads to uncontrolled lipolysis and elevated levels of free fatty acids in the plasma, which suppresses glucose metabolism in peripheral tissues such as skeletal muscle .This impairs glucose utilization and insulin deficiency also decreases the expression of a number of genes necessary for target tissues to respond normally to insulin

PATHOPHYSIOLOGY OF TYPE-II DM


Genetics
Acquired
Insulin resistance
Hyperinsulinemia
Compensated insulin resistance
IGT
Islet B cell failure
• Genetics
• Glucotoxicity
• Lipotoxicity (FFAs)
• Other
Type 2 diabetes
• Insulin resistance
• ↑ HGO
• ↓ Insulin secretion

- the two main pathological defects in type 2 diabetes are impaired insulin secretion through a dysfunction of the pancreatic ß-cell, and impaired insulin action through insulin resistance
- the plasma insulin concentration (both fasting and meal stimulated) usually is increased, although "relative" to the severity of insulin resistance, the plasma insulin concentration is insufficient to maintain normal glucose homeostasis.

- Insulin resistance and hyperinsulinemia eventually lead to impaired glucose tolerance
- To overcome the insulin resistance, islet cells will increase the amount of insulin secreted. Endogenous glucose production is accelerated in patients with type 2 diabetes or impaired fasting **glucose** Because this increase occurs in the presence of hyper insulinemia, at least in the early and intermediate disease stages, hepatic insulin resistance is the driving force of hyperglycemia of type 2 diabetes

COMPLICATIONS

SHORT TERM	LONG TERM
• Ketoacidosis •Non ketotic coma (severe dehydration due to continuous loss of glucose in urine) •Hypoglycemia (reduced glucose level in blood)	**MACROVASCULAR** •Atherosclerosis •Diabetic microangiopathy (thickening of basement membrane of blood vessels) **MICROVASCULAR** •Diabetic nephropathy (damage to kidneys) •Diabetic neuropathy (damage to nerves) •Diabetic retinopathy (damage to retina)