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DIABETES AND ITS COMPLICATIONS: MOLECULAR MECHANISMS AND THERAPEUTIC STRATEGIES

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Abstract: Diabetes mellitus is one of the most prevalent metabolic disorders worldwide and represents a major global health challenge.
The disease is characterized by chronic hyperglycemia caused by impaired insulin secretion, insulin resistance, or both. Long-term hyperglycemia leads to numerous complications affecting different organs and physiological systems. These complications include diabetic nephropathy, retinopathy, neuropathy, and cardiovascular diseases. Recent biomedical research emphasizes the importance of molecular and cellular mechanisms involved in the development of diabetic complications. Chronic inflammation, oxidative stress, endothelial dysfunction, and metabolic imbalance are considered the key factors responsible for tissue damage in diabetic patients. Understanding these mechanisms is essential for developing effective therapeutic strategies and preventing disease progression.

Introduction: Diabetes mellitus is a chronic metabolic disease characterized by elevated blood glucose levels. It results either from insufficient insulin production by pancreatic β-cells or from reduced sensitivity of peripheral tissues to insulin. Over the past decades, diabetes has become a major public health concern because of its rapidly increasing prevalence worldwide.

Persistent hyperglycemia is responsible for long-term damage to multiple organs including the kidneys, eyes, nerves, heart, and blood vessels. As a consequence, diabetic complications significantly reduce quality of life and increase mortality rates among affected individuals. Modern research has shown that the development of these complications is not only related to high glucose levels but also to a complex interaction of metabolic and molecular processes.

Molecular Mechanisms of Diabetes

At the molecular level, diabetes involves several metabolic disturbances that disrupt normal cellular homeostasis. One of the most important processes is insulin resistance, a condition in which cells fail to respond adequately to insulin signaling. Insulin resistance leads to reduced glucose uptake in muscle and adipose tissue and increased glucose production in the liver.

Chronic hyperglycemia activates several biochemical pathways including the polyol pathway, the formation of advanced glycation end products (AGEs), activation of protein kinase C, and increased oxidative stress.
These mechanisms contribute to vascular dysfunction and cellular damage. Oxidative stress in particular plays a crucial role by increasing the production of reactive oxygen species that damage proteins, lipids,
and DNA.

The Ominous Octet Concept

The pathophysiology of type 2 diabetes was further clarified through the concept known as the "ominous octet." This model describes eight key physiological defects responsible for the development and progression of the disease. These mechanisms include impaired insulin

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secretion, increased glucagon production, insulin resistance in muscles, increased hepatic glucose production, decreased incretin effect, increased lipolysis in adipose tissue, increased renal glucose reabsorption, and central nervous system dysregulation.

Together these abnormalities maintain chronic hyperglycemia and accelerate the development of diabetic complications. Understanding these mechanisms has allowed researchers to develop targeted therapies that
address specific metabolic defects rather than focusing solely on glucose reduction.

Microvascular Complications

Microvascular complications affect small blood vessels and are among the most common consequences of long-standing diabetes. Diabetic retinopathy is a major cause of vision loss and occurs due to damage to retinal capillaries. The condition is characterized by microaneurysms, vascular leakage, and retinal ischemia.

Diabetic nephropathy is another serious complication that results from damage to the kidney filtration system. Structural changes in the glomeruli lead to progressive decline in kidney function. Without proper treatment this condition may progress to end-stage renal disease.

Peripheral neuropathy is caused by metabolic and vascular injury to peripheral nerves. Symptoms include pain, numbness, and loss of sensation, particularly in the lower extremities. Severe neuropathy increases the risk of foot ulcers and infections.

Macrovascular Complications

Macrovascular complications involve large blood vessels and represent the leading cause of mortality in diabetic patients. Chronic hyperglycemia contributes to endothelial dysfunction and accelerates atherosclerosis. These processes increase the risk of coronary artery disease, myocardial infarction,
stroke, and peripheral artery disease.

Cardiovascular complications are particularly significant because they often develop silently over many years before clinical symptoms appear. Early prevention strategies including glycemic control, lipid
management, and blood pressure regulation are essential to reduce cardiovascular risk.

Therapeutic Strategies

Management of diabetes requires a comprehensive approach that combines lifestyle interventions and pharmacological therapy. Healthy diet, regular physical activity, and weight management are fundamental components of treatment.

In recent years several novel classes of antidiabetic medications have been introduced. Sodium-glucose cotransporter-2 (SGLT2) inhibitors reduce glucose reabsorption in the kidneys and have demonstrated cardiovascular and renal protective effects. Glucagon-like peptide-1 (GLP-1) receptor agonists enhance insulin secretion and improve metabolic regulation.

In addition to pharmacological treatment, early detection of complications through regular screening is essential for preventing irreversible organ damage.

Conclusion

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Diabetes mellitus is a complex metabolic disorder associated with numerous systemic complications. Persistent hyperglycemia combined with metabolic and inflammatory disturbances leads to progressive damage of multiple organs. Advances in molecular biology have significantly improved understanding of the mechanisms responsible for diabetic complications.

Modern therapeutic strategies increasingly focus on targeted treatments that address the underlying metabolic defects described in the "ominous octet." Continued research and early intervention are essential for reducing the global burden of diabetes and improving patient outcomes.

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