Unit IV – Problem 1 – Immunology: Type-I Diabetes

- **Type-I diabetes is classified into:**
  - **Type-IA**: which is autoimmune (there are autoantibodies causing destruction of β-cells in islets of Langerhans).
    - ✓ This attack if mediated by activated cytotoxic T-cells which are leading to a condition known as insulitis.
  - **Type-IB:** insulin deficiency without the presence of autoantibodies.
- **Type-I diabetes mostly affects children and is known as (juvenile). When it affects adults, it will be known as (latent).**
- **Risk factors of diabetes type-I:**
  - There must be a genetically predisposed person with environmental trigger (such as a viral infection or damage to β-cells) resulting in immune response against normal β-cells (destruction).
- **Stages in development of diabetes type-I:**
  - Genetic predisposition → insulitis (mediated by T-cell-mediated) → pre-diabetes → diabetes
- **HLA-system (=MHC):**
  - **There are two types of MHC complexes:**
    - ✓ Type 1: present on all nucleated cells of the body and reacting with cytotoxic T-cells. Composed of: HLA-A, HLA-B and HLA-C
    - ✓ Type 2: present on antigen-presenting cells (macrophages, B-lymphocytes and dendritic cells). Composed of: HLA-DQ, HLA-DR and HLA-DP.
    - ✓ Diabetes type-1 is associated with: HLA-DR3 and HLA-DR4
- **What are the B-islet cells autoantigens?**
  - **Glutamate decarboxylase (GAD):** higher sensitivity in adult onset type-1A
  - **Insulin (IAA):** higher sensitivity in young children.
  - **Islet antigen-1 (IA-2).**
  - **Zinc transporter-8 (ZnT8).**

    These markers are usually inside the β-cell, but when it is destroyed, they will be out in the blood stream and antibodies will form against them. Antibodies can be detected in early stages of the disease, but at late stages they are not detected simply because β-cells are destroyed and the antigens will disappear.
- **Clinical onset of diabetes type-1 begins when 80% of β-cells are destroyed.**
- **Type-I vs. type-II diabetes mellitus:**

Variable	Type 1	Type 2
Primary defect	Autoimmune destruction of β-cells	↑ resistance to insulin, progressive pancreatic β-cell failure
Insulin necessary in treatment	Always	Sometimes
Age	< 30 years	> 40 years
Association with obesity	No	Yes
Genetic predisposition	Relatively weak	Relatively strong
Association with HLA-system	Yes (HLA-DR3 and DR4)	No
Glucose intolerance	Severe	Mild to moderate
Insulin sensitivity	High	Low
Ketoacidosis	Common	Rare
Histology	Islet leukocytic infiltrate	Islet amyloid polypeptide deposits