Unit II – Problem 6 – Immunology: Delayed-Type Hypersensitivity

- **Define hypersensitivity diseases.**
  - **These are conditions in which tissue damage is caused by immune responses:**
    - ✓ Excessive responses to foreign antigens.
    - ✓ Failure of self-tolerance (autoimmunity).
- **Hypersensitivity is classified according to the effector mechanism responsible for tissue injury. Four types are commonly recognized:**

Type of hypersensitivity	Immune mechanisms	Mechanisms of tissue injury
Type-I (immediate)	IgE	Mast cells and their mediators (in addition to basophils and eosinophils)
Type-II (antibody-mediated)	IgM and IgG antibodies against cell or tissue antigens	Opsonization and phagocytosis of cells; complement and Fc receptor mediated recruitment and activation of neutrophils and macrophages; abnormalities in cellular functions (hormone/receptor signaling)
Type-III (immune complex-mediated)	Immune complexes of circulating antigens and IgM or IgG antibodies	Complement and Fc receptor mediated recruitment and activation of leujocytes
Type-IV (delayed-type hypersensitivity)	CD4+ TH1 and TH17 cells, their cytokines and the cells of CMI that they stimulate	• Macrophages activation, cytokine-mediated inflammation (granuloma formation) • CD8+ CTLs (T-cell-mediated cytolysis) • direct target cell killing, cytokine-mediated inflammation

- **Type-IV (T cell-mediated) hypersensitivity:**
  - **T-lymphocytes may cause tissue injury by triggering delayed-type hypersensitivity (DTH) reactions or by directly killing target cells. These reactions are elicited by CD4+ TH1 and TH17 cells and CD8+ cells which activate macrophages (IFN-γ), recruit neutrophils (IL-17 and IL-23) and induce inflammation (TNF). These T-cells may be autorective or specific against foreign protein antigens bound to tissues. T-cell-mediated tissue injury is common during the protective immune response against persistent intracellular microbes.**
  - **Summary of type-IV hypersensitivity:**
    - ✓ Delayed-type (48 to 72 hours).
    - ✓ Mediated by: CD4+ TH1 cells.
    - ✓ Macrophages are activated.
    - ✓ Inflammation results.
    - ✓ Common in chronic intracellular infections.
- **Examples of type-IV hypersensitivity:**

Disease	Specificity of pathogenic T-cells	Clinical manifestations
Tuberculin test	PPD (tuberculin and mycolic acid)	Indurated skin lesion (granuloma)
Hashimoto thyroiditis	Unknown antigen in thyroid gland	Hypothyroidism
Multiple sclerosis	Myelin basic protein	Progressive demyelination, blurred vision, paralysis
Insulin-dependent diabetes mellitus (type-I)	Islet-cell antigens, insulin, glutamic acid decarboxylase and others	Chronic inflammation and destruction of β-cells, polydipsia, polyuria, polyphagia & ketoacidosis