

7.6 Autoimmunity and tolerance

Name: _____ Class: _____ Date: _____ **Total: 23 marks**

KEY WORDS central tolerance

Objective

Trace autoimmunity to failed checkpoints and interpret twin and serology data.

1 Key knowledge and worked examples

■ The filters

Central: deletion + Treg breeding. Peripheral: anergy, suppression ✓. AIRE → polyglandular; FOXP3 → IPEX.

■ Worked example: the numbers

T1D identical-twin concordance 30–50 % ✓; low-positive ANA in 5–15 % of healthy adults.

2 Practice

2.1 Where does central tolerance act? [3]

2.2 Name the Treg master gene. [3]

2.3 What triggers molecular mimicry in rheumatic fever? [3]

3 Exam-style questions

3.1 A 4-year-old has chronic eczema, diarrhoea and early-onset diabetes (fictional IPEX picture).

Name the failed checkpoint (FOXP3 → Treg). Explain why SKIN and GUT bear the brunt (barrier surfaces need active suppression). State the inheritance and the treatment direction. [7]

3.2 A healthy 24-year-old woman is found ANA-positive at low titer on a screening panel (fictional).

Interpret the finding (5–15 % healthy prevalence). State what would raise suspicion (high titer, specific patterns – dsDNA, anti-Sm). Explain the twin logic (30–50 % concordance) for why HLA typing is probabilistic, not deterministic. [7]

Solutions

2.1

- Thymus and marrow.

2.2

- FOXP3 ✓.

2.3

- Streptococcal infection (antibodies cross-reacting with heart and joint).

3.1

- FOXP3 failure: no functional Treg – the peripheral filter is gone.
- Barrier surfaces (skin, gut) host abundant self-reactive and commensal-reactive clones held by active suppression: they fail first ✓.
- X-linked; treatment direction = immune suppression $\pm$ bone-marrow transplant (restores Treg lineage).

3.2

- Low-positive ANA: 5–15 % of healthy adults – not diagnostic ✓.
- Suspicion: high titer + patterns (anti-dsDNA, anti-Sm for SLE, with corresponding clinical criteria).
- 30–50 % identical-twin concordance: HLA sets thresholds; the trigger is environmental/stochastic ✓.