QUESTION 32

An 18 year old woman with type 1 diabetes mellitus is at most risk of developing which of the following conditions?

A. Addison’s disease  
B. Pernicious anaemia  
C. Hashimoto’s thyroiditis  
D. Primary ovarian failure  
E. Systemic lupus erythematosus

PATHOGENESIS OF T1DM

- T1DM results from autoimmune destruction of the insulin-producing beta-cells in the islets of Langerhans.
- Occurs in genetically susceptible individuals and is probably triggered by environmental agents.
- Long latent period where pt is asymptomatic and euglycaemic.
- Type 1B diabetes mellitus refers to non-autoimmune islet destruction.
- Six genes are known to influence the risk of T1DM.
- One of these genes codes for MHC class II molecules to which antigens involved in the pathogenesis of T1DM bind.
- Allows antigen to be presented to T cells which are the main effector cell in the process.
- Islet cell autoantibodies (ICAs) are present in 70-80% of pts w T1DM.
- Autoantigens include glutamic acid decarboxylase which is present in the islets. Autoantibodies to GAD are found in 70% of pts w T1DM.
- Also insulin and proinsulin autoantigens/autoantibodies, insulinoma-associated protein 2 autoantigens/autoantibodies.
- B cells may play a role in the development of T1DM but are not essential to the process.

- T1DM associated with other autoimmune disorders:
  - Thyroid autoimmunity (1 in 4)
  - Antiadrenal antibodies and adrenal insufficiency (about 1-2%)
  - Polyglandular autoimmune disease (adrenal insufficiency, autoimmune thyroid disease and gonadal insufficiency are major components)
Transglutaminase autoantibodies in ~ 10%, coeliac disease on Bx in about half of these (most asymptomatic)

IPEX is a rare syndrome of overwhelming autoimmunity in neonates. Usually die of severe enteritis. Mutation of foxp3 (gene for regulatory T cells)

Autoimmune polyendocrine syndrome type 1 is caused by a mutation of AIRE gene (autoimmune regulator), which normally provides protection from autoimmunity

- Environmental factors
  - Perinatal factors (eg: age >25, pre-eclampsia, neonatal resp disease, jaundice)
  - Viruses may play a role (eg: Coxsackievirus, enterovirus)
  - Dietary (eg: cow’s milk, timing of exposure to cereals)