Endocrine VIVAs (Pathology)

shakEM

Aug 2015

2015.1.C.2

Question 1 Pathogenesis of Diabetes Mellitus **Subject:** Path LOA: 2	What is the pathogenesis of Type 2 Diabetes Mellitus?	**Insulin resistance** - decreased ability of the peripheral tissues to respond to the secreted insulin - secondary to either genetic predisposition or obesity/lifestyle factors Quantitative and qualitative **beta cell dysfunction** - manifests as inadequate insulin secretion in the face of insulin resistance and hyperglycaemia - initial beta cell hyperplasia maintains normoglycaemia with increased levels of insulin secretion - early and subsequently late failure manifests as impaired glucose tolerance and diabetes - genetic predisposition to B-cell failure.	Bold to pass
	What are the complications of diabetes?	1. **Macrovascular** - coronary, peripheral vascular, cerebral and other large vessel atherosclerosis, hypertension 2. **Microangiopathy**- nephropathy, peripheral neuropathy, autonomic neuropathy, cerebral microangiopathy 3. **Diabetic ocular complications**- retinopathy, cataracts, glaucoma 4. Increased susceptibility to infections 5. HONK, DKA, hypoglycaemia, hyperglycaemia	Two from 1 & 2 and one from the third group.

2014.1.C.1

Question 4 Complications of diabetes mellitus (Robbins pp1138-1143) **Subject:** Path	a) What are the principal complications of Diabetes mellitus? (Prompt: what happens in the pancreas?)	**Vascular-** **- macro** atherosclerosis, CAD, PVD, RAS, HT and CVA - **microangopathic** thickened BM, increased permeability of capillaries to plasma proteins - nephropathy, retinopathy, neuropathy	Bold + 3 of 7 clinical complications.
LOA: 2	b) Outline some of the differences in patients with Type 1 and type 2 diabetes.	**Pancreatic changes** - loss of islets cells (number and size), amyloid infiltration of islets Renal - sclerosis, BM thickening, glomerulosclerosis Occular- prolif and non prolif, haemorrhages, exudates neovascularisation, detachment, glaucoma Neuropathy	Question b (to pass) - age group and severity of illness + at least 2 symptoms or syndromes associated with each type. Age + 2 clinical + 1 pathology to pass

Type 1	Type 2
Onset: childhood, <18	Onset: usually adult
N or under weight	Obese
Dec in insulin	Inc blood insulin
Circulating islet autoantibodies	No islet auto-antibodies
polyuria, polydipsia, polyphagia +/- ketoacidosis	May have HONC
Genetic linkage	No genetic linkage
Dysfunction in T cell resulting in islet Ab	Insulin resistance

Type 1 :-
- typically young < 18 yrs, usually abrupt onset due to exhaustion of b cell reserve - often with a precipitating illness increasing demands on pancreas eg. infection-

Type 2 :-
- often > 40 yrs, obese
- often asymptomatic and incidental finding on routine followup or bloods
- may have DKA or HONC with dehydrating precipitant
- often a longer cause illness due to residual pancreas capacity

2011.2.3

Question 4 LOA: 2	1.What is the pathogenesis of Type 2 Diabetes Mellitus?	**1.Insulin resistance** - decreased ability of the peripheral tissues to respond to the secreted insulin - secondary to either genetic predisposition or obesity/lifestyle factors Quantitative and qualitative **beta cell dysfunction** - manifests as inadequate insulin secretion in the face of insulin resistance and hyperglycaemia - initial beta cell hyperplasia maintains normoglycaemia with increased levels of insulin secretion - early and subsequently late failure manifests as impaired glucose tolerance and diabetes - genetic predisposition to B-cell failure.	Bold to pass
	2.What are the of the principal complications of Type 2 Diabetes Mellitus ?") (Prompt what is the common underlying pathological process?)	**2.Vascular** **Diabetic macrovascular disease-** Accelerated atherosclerosis, CAD, PVD, Renal arteriosclerosis. **Hyaline arteriosclerosis-** Hypertension 1& 2 leading to CVA **Diabetic microangiopathy-** diffuse thickening of the basement membrane- (increased concentric hyaline material type 4 collagen) + increased permeability of the of the diabetic capillaries to plasma proteins- diabetic nephropathy, retinopathy and neuropathy. **Renal** **Diabetic nephropathy**- glomerular lesions- BM thickening, diffuse mesangial sclerosis and nodular glomerulosclerosis- **nephrotic syndrome**, Renal atherosclerosis and arteriolosclerosis Pyelonephritis/necrotising papillitis **Ocular**	**microangiopathy vascular, renal and 1 other** complications
		Diabetic Retinopathy- Proliferative and non proliferative- micronaneurysms, haemorrhages, soft and hard exudates, retinal venous dilatation and oedema, neovascularisation, fibrosis- vitreous haemorrhage and retinal detachment Cataracts Glaucoma **Neuropathy**	

2009.2

Question 1: Diabetes Mellitus Type 1	What is the pathogenesis of diabetic ketoacidosis?	1. **Insulin deficiency** and glucagon excess →decreases peripheral utilization of glucose while increasing gluconeogenesis → severe **hyperglycaemia** 2. Hyperglycaemia causes **osmotic diuresis** and dehydration 3. Insulin deficiency increases **lipolysis and FFAs production**. FFAs are converted to **ketone bodies** by the liver. If rate of ketone bodies production exceeds rate of utilization by peripheral tissues→ketonaemia and ketonuria. Decreased urinary excretion of ketones leads to systemic metabolic ketoacidosis	1 from each of these groups to pass
Question 2:	What are the long-term complications of diabetes?	1. **Macrovascular**- coronary, peripheral vascular, cerebral and other large artery atherosclerosis, hypertension 2. **Microangiopathy**- nephropathy, cerebral microangiopathy, peripheral neuropathy, autonomic neuropathy 3. **Diabetic ocular complications**- retinopathy, cataracts, glaucoma	Macrovascular and microvascular with 2 examples of each to pass **or** Simple list of 6 to pass Higher score for organization in groups
Question 3:	Describe the stages in the development of Type 1 Diabetes?	1. Genetic predisposition 2. Precipitating event 3. Autoimmune destruction of islet cells 4. Subclinical leading to overt DM	Optional part of qn.

2008.2

5.Thyrotoxicosis	1.What is thyrotoxicosis?	Hypermetabolic state caused by elevated circulating levels of T_3 and T_4	Need to know
	2. What are the clinical features of thyrotoxicosis?	**Cardiac –** inc HR, dysrhythmias, CCF Neuromusc – tremor, prox myopathy **Ocular –** wide staring gaze, lid lag, proptosis CNS – anxiety, emotional lability, insomnia Skin – warm, flushed, inc sweating **Heat intolerance** **Thyroid storm –** fever, tachycardia, arrhyth., may be fatal if not treated promptly	Highlighted
	3. What are the main causes of thyrotoxicosis?	**Diffuse toxic hyperplasia (Graves disease)** Toxic multinodular goitre Toxic adenoma/carcinoma Neonatal from maternal Graves dis Non-hyperthyroidism – thyroiditis, etc	Highlighted + 1 other

2008.2

Question 5: Pathogenesis of Type 1 Diabetes Mellitus	1. What is the pathogenesis of Type 1 Diabetes Mellitus	1. Genetic predisposition 2. Precipitating event 3. Autoimmune destruction of islet cells 4. Subclinical leading to overt DM	3 to pass
	2. What environmental factors may contribute to the development of Type I Diabetes Mellitus?	1. Infections (group B coxsackieviruses; mumps; measles; CMV; rubella; EBV): may induce tissue damage and inflammation, leading to the release of B-cell antigens. ***OR*** the viruses produce antigens which mimic self-antigens with the immune response cross-reacting with self-tissue.	
	3. How does genetic susceptibility contribute to the development of Type I DM?	2. Complex pattern of genetic associations: putative susceptibility genes mapped to at least 20 loci. Most important is ***class II MHC (HLA) locus → 50% of total*** genetic susceptibility: on chromosome 6p21 (HLA-D) 95% Caucasians with type I DM have HLA-DR3, DR4 or both. ***DQB1*0302 allele considered the primary determinant of genetic susceptibility***. **Non-MHC genes**: the first disease-associated non-MHC gene to be identified was *insulin*. Tandem repeats in the promoter region being associated with disease susceptibility. • **mechanism of association is unknown**: maybe the disease associated polymorphism makes the protein less functional or stable OR may influence the level of expression of insulin in the thymus, so altering negative selection of insulin-reactive T cells Another gene recently shown to be associated: encoding for the T-cell inhibitory receptor CTLA-4	