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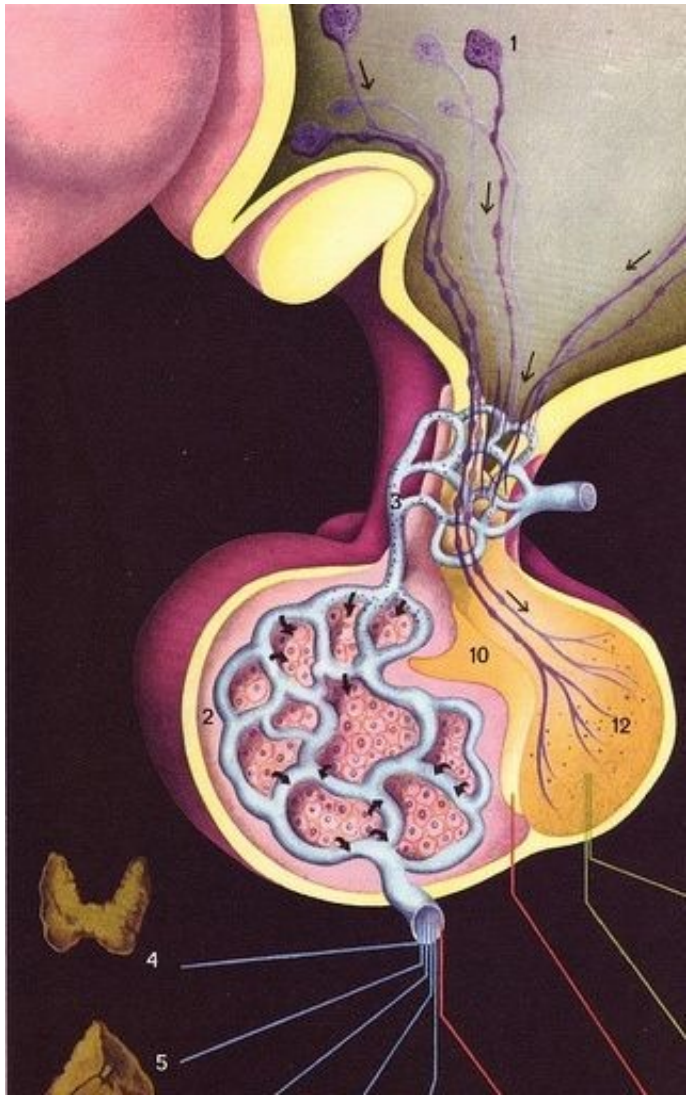

Diabetes Mellitus 2014-1-C

<table>
<tr><td colspan="4">Stem: We now move onto pathology.</td></tr>
<tr><td>Question 4
Complications of diabetes mellitus (Robbins pp1138-1143)

Subject: Path</td><td>a) What are the principal complications of Diabetes mellitus?
(Prompt: what happens in the pancreas?)</td><td>Vascular-
- macro atherosclerosis, CAD, PVD, RAS, HT and CVA
- microangopathic thickened BM, increased permeability of capillaries to plasma proteins - nephropathy, retinopathy, neuropathy</td><td>Bold + 3 of 7 clinical complications.</td></tr>
<tr><td>LOA: 2</td><td>b) Outline some of the differences in patients with Type 1 and type 2 diabetes.</td><td>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

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

<u>Type 2 :-</u>
- 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</td><td>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</td></tr>
</table>

Diabetes Mellitus DKA 2009-2

TOPIC	QUESTION	ESSENTIAL KNOWLEDGE	NOTES
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.

Diabetes Mellitus Type 1 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	

Diabetes Mellitus Type 1 2006-1

TOPIC: Pathophysiology of Diabetes Mellitus Type I_____ **NUMBER:** _____

OPENING QUESTION	What are the main risk factors for the development of Type I Diabetes Mellitus	**COMMENTS**
POINTS REQUIRED	1 Genetic factors - Northern European decent, familial groupings, identical twin concordance rate 70%, 6% in first degree relatives, linked to class II antigens of major histocompatability complex	At least (1) plus one other to pass
	2 Viral infections - cocksackie B, mumps, measles, CMV, rubella, EBV	
	3 Cows milk exposure prior to 4 months of age	
	4 Drugs - pentamidine	
PROMPTS		
SECOND QUESTION (if needed)	What is the sequence of events that leads to Type I diabetes mellitus?	
POINTS REQUIRED	1 Genetic susceptibility	At least 3 to pass
	2 Exposure to environmental insult - exogenous antigen (viral), drugs	
	3 Auto immune response directed towards beta cells - molecular mimicry or altered expression of Beta cell antigens, 70-80% have auto islet antibodies	
	4 Beta cell destruction - reduced cell mass and insulin	
	5 Hyperglycaemia	
PROMPTS	How do the risk factors combine to cause Type I DM?	
THIRD QUESTION (if needed)	What are some of the long-term complications of chronic hyperglycaemia?	At least 3 to pass
POINTS REQUIRED	1 Vascular - macro and microvascular, CVasc, renal, ocular	
	2 Neuropathic	
	3 Immune	
	4 Renal- Kimmelstiel Wilson lesions	
	5 Foetal	
	6 Dermal - ulcers, necrobiosis	
	7 Muscular - proximal myopathy	
PROMPTS		

Diabetes Mellitus Type 2 2015-1-C

Stem: A 60 yo man has a very high blood glucose. We will start with Pathology.			
TOPIC	QUESTIONS	KNOWLEDGE **(essential in bold)**	NOTES
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.

Diabetes Mellitus Type 2 2011-2

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** **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**	**microangiopathy vascular, renal and 1 other** complications

Diabetes Mellitus Type 2 2006-1

TOPIC: Pathophysiology of Diabetes Mellitus Type II ____ **NUMBER:** _____

OPENING QUESTION	What defects in glucose handling characterise Type II Diabetes Mellitus?	**COMMENTS**
POINTS REQUIRED	1 Reduced insulin secretion from beta cells - altered glucose sensing mechanism, cellular overstimulation	2 to pass with basic mechanisms
	2 Reduced tissue responsiveness to insulin - reduced post receptor signaling, reduced insulin receptors	
PROMPTS	What are the mechanisms?	
SECOND QUESTION (if needed)	What are the main risk factors for the development of Type II diabetes mellitus?	
POINTS REQUIRED	1 Obesity (most important) - present in 80%, truncal obesity higher risk,	At least 1 to pass
	2 Genetic factors - not HLA linked, collection of multiple genetic defects, more important than Type I DM, concordance rates in identical twins 60-80%	
PROMPTS		
THIRD QUESTION (if needed)	What are the main adverse effects of acute, severe, sustained hyperglycaemia?	
POINTS REQUIRED	1 Osmotic diuresis - hypovolaemia, risk of thrombosis	At least 2 to pass
	2 Electrolyte losses - Na, K, PO4	
	3 Hyperosmolarity - changes in conscious state	
PROMPTS		

Graves Disease 2006-1

TOPIC: Friday AM – Q 2 – Graves Disease _____ **NUMBER:** _____

OPENING QUESTION	What are the characteristic clinical findings of Grave's disease?	**COMMENTS**
POINTS REQUIRED	1. Clinical hyperfunction	First 2 to pass
	2. Thyroid enlargement	
	3. Infiltrative opthalmopathy	
	4 Infiltrative dermopathy	
PROMPTS		
SECOND QUESTION (if needed)	What is the pathogenesis?	At least 2 to pass
POINTS REQUIRED	1. Auto-immune: variety of antibodies	
	2. Auto-antibodies to TSH receptors	
	3. LATS – IgG mimics TSH, thyroid stimulating immunoglobulin	
	4.	
PROMPTS		

Pituitary Adenomas 2008-2

5. Pituitary Adenomas:	1. How are pituitary adenomas classified? Prompt: Name two cell types involved.	Classification based on **hormone cell-type**: prolactin cell, growth hormone cell (densely or sparsely granulated), thyroid stimulating cell, ACTH cell, gonadotroph cell (including silent and oncocytic), mixed GH-prolactin cell, Other plurihormonal cell, hormone negative.	Highlighted & 2 cell types to pass. If describe "functional" or "silent" adenomas – move to prompt
	2. What clinical syndromes may they produce?	Prolactinoma: amenorrhea, galactorrhea, loss of libido, and infertility Somatotroph (GH): gigantism or acromegaly ACTH: Cushing's syndrome Gonadotroph: local effects (headaches, visual impairment, diplopia, pituitary apoplexy), hypogonadism (lethargy, loss of libido, amenorrhoea)	

Thyrotoxicosis 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