Endocrine Block Final Revision

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Adrenal gland.

	Disorder	Clinical features	Causes	morphology	Diagnosis
	Adrenal cortex				
HYPERFUNCTION	**Cushing syndrome**	- Moon face. - Buffalo hump. - Hypertension. - Central obesity. - Osteoporosis. - Hirsutism. - Abdominal striae. - Hyperglycaemia - Plethora.	- Exogenous glucocorticoid "iatrogenic". - ACTH-secreting pituitary adenoma. - Ectopic ACTH secretion (e.g. Small cell carcinoma of the lung). - Primary adrenal neoplasm.	1. **Cortical atrophy:** results from exogenous glucocorticoids 2. **Diffuse hyperplasia:** individuals with ACTH-dependent Cushing syndrome.	**Serum ACTH:** - Low → adrenal neoplasms. - High → pituitary adenomas and ectopic ACTH. **High dose dexamethasone suppression test:** - Low → pituitary adenomas. - High → ectopic ACTH.
	Hyper-aldosteronism "Conn syndrome"	- Hypertension. - Hypokalemia. - Hypernatremia. - Metabolic alkalosis. - Muscular weakness.	- Adenoma of the zona glomerulosa. - Bilateral adrenal hyperplasia (rare).	- Solitary, Small. - well circumscribed lesions. - No visible enlargement. - Bright yellow on cut section.	↑ Aldosterone. ↓ Renin. (if the renin levels are raised, then the hyperaldosteronism is secondary)
HYPOFUNCTION	**Acute adreno-cortical insufficiency** "adrenal crisis"	- Hypovolaemic shock. - Hypoglycaemia due to lack of glucocorticoids.	- Rapid steroid treatment withdrawal. - Destruction of the adrenal glands by hemorrhage , which can be complicate bacterial (e.g.meningococcal), Waterhouse-Friderichsen syndrome.	**Waterhouse-Friderichsen syndrome:** Gross: hemorrhage and shrinkage. Microscopically: little residual cortical architecture is discernible.	--
	Chronic adreno-cortical insufficiency "Addison disease"	- Weakness. - Weight loss. - Hypotension - Dehydration. - Hyper-pigmentation. - Hyponatraemia - Hyperkalaemia - Hypoglycaemia.	Autoimmune destruction of the adrenal cortex	--	**Synacthen tests:** - ↑ Cortisol levels → normal. - ↓ Cortisol levels → primary or secondary adrenocortical insufficiency. - Long Synacthen test should then be performed.

	Secondary adreno-cortical insufficiency		- Primary lesions of the pituitary. - Hypothalamic-pituitary-adrenal suppression as a result of long-term steroid therapy	--	Long Synacthen test
	Adrenal medulla				
T U M O R	**Pheochromocytoma**	- Young hypertensive patient. - Palpitations. - Pallor.	Associated with familial syndromes such as: - MEN syndrome. - Von-Hippel-Lindau disease. - Von Recklinghausen's disease.	- Small to large hemorrhagic - Well demarcate - Polygonal to spindle shaped (**chromaffin**, chief cells). - Sustentacular small cells. - Zellballen nests.	Urinary excretion of the catecholamine metabolite vanillylmandelic acid (VMA). Which is at least doubled.

Extra:

Table 2. Selected Endocrine Paraneoplastic Syndromes.

Clinical Presentation	Hormone	Most Common Responsible Tumors
Cushing's syndrome	Corticotropin or corticotropin-releasing hormone	Small-cell carcinoma of the lung, carcinoid tumors, medullary thyroid carcinoma, pheochromocytoma
Hypercalcemia	Parathyroid hormone–related peptide	Squamous-cell carcinoma of the lung, skin, head and neck; renal carcinoma; carcinoid tumors

Diabetes.

Characteristic	TYPE 1 **insulin-dependent (IDDM)** **or juvenile-onset diabetes.**	TYPE 2 (More common) **non–insulin-dependent (NIDDM)** **or maturity-onset diabetes.**
Age at onset	Children, Peak at puberty	Adult >35 years
Speed of onset	Rapid	Gradually
BMI	Usually thin	Usually obese (80% of cases)
Genetics	● Moderately associated Family history ● MHC11 6p21 HLA-DR3 and HLA-DR4	● Strongly associated Family history ● No MHC-HLA association
Pathogenesis	Genetic susceptibility + Environmental factors such as (Coxsackievirus) → Autoimmunity → T lymphocytes + IL-1, IL-6, interferon-alpha, and nitric oxide, lead to → to B cell injury→ insulin deficiency→ Diabetes.	Genetic + Environmental (as obese) → downregulation of Insulin receptor→ insulin resistant → compensation by hyperinsulinemia → Beta cells get exhausted or destructed by cytokines released from FFA → Diabetes.
Symptoms	● Polyuria, Polydipsia, Polyphagia, weight loss ● Glucosuria, muscle weakness, malaise, fatigue. ● Recurrent blurry vision: alteration in lens refraction from sorbitol ● Recurrent infections: bacterial, Candida	
Morphology	1. Insulitis: Lymphocytic infiltrate in islets. 2. B-Cell: Markedly reduced 3. Exocrine: Fibrosis & atrophy of the acinar cells.	1. **Islet amyloid.** (Congo Red stain) 2. B-Cell: Normal or slightly reduced. 3. Endocrine: Islets Fibrosis
	Ketoacidosis: insulin is deficiency and glucagon is high → ketogenesis more than ketolysis → ketonemia → ketonuria **Characterized by:** hyperglycemia, dehydration, low K and metabolic acidosis.	**HNKC:** enough insulin to prevent ketoacidosis but not enough to prevent hyperglycemia Lactic acidosis may occur from shock (losing sodium by osmotic diuresis from glucosuria)
Treatment	Insulin	Diet, Exercise, OHG, Insulin, Reduce the risk factors (BP, Smoking.. etc)

Other types of diabetes.	
MODY (Maturity-onset diabetes of the young) (T3DM)	● **Resembles type 2 DM, but occurs in young age group.** ● **Rare *autosomal dominant* diabetes,** ● **It has very strong family history** ● **Associated with a variety of gene defects in function or structure of beta cell.** ● **Caused by mutation in: HNF,GCK,PDX1,NEUROD1**
Secondary (T4DM)	● **Secondary to other endocrine conditions (Cushing's syndrome, pheochromocytoma, chronic pancreatitis or pancreatic cancer) or drug therapy (ex: Beta-blockers, glucocorticoids)** ● **Exocrine pancreatic defect:** chronic pancreatitis, neoplasia, cystic fibrosis. ● **Infection:** CMV,Coxsackie B virus, congenital rubella. ● **Genetic syndrome:** Down's, klinefelter , Turner , prader-Willi syndromes.
Gestational diabetes	● **few percent of healthy pregnant women, due to the insulin resistance of pregnancy combined with B -cell defect** ● **almost always abates following parturition.** ● **May Put both Mother and Fetus at risk.** ● **These women highly susceptible to overt T2DM later in life.**

Complications of Diabetes Mellitus

Pathogenesis:

- **Occlusion** of vessels by non-enzymatic glycosylation of protein→ ischemia.
  - Microvascular→ hyaline arteriosclerosis
  - Macrovascular → atherosclerosis
- **Osmotic damage:** secondary to hyperglycemia→ increase intracellular osmotic pressure→ osmotic drag of fluid from ECF→ swelling→ cell damage.

Nephropathy	- Renal failure **due to nodular glomerulosclerosis.** - Nephrotic syndrome **due kimmelstiel Wilson disease** - **T1DM >T2DM** - Most cases of renal failure and renal transplantation.
Retinopathy	- Cataract or Blindness - Risk T1DM>T2DM but more common in T2DM
Neuropathy	- burning and abnormal sensation - Affect sensory nerves→ foot ulcer - Affect Autonomic nerve→ infection (urinary retention) - Painless destructive joint disease.
Infection	❑ **Renal papillary necrosis** → complication of bladder infection. ❑ **Mucormycosis**: → complication of poorly controlled diabetes → fatal fungal infection originate in the nasopharynx or paranasal sinuses and spreads rapidly to the orbit and brain. ❑ **Cellulitis**: infection of subcutaneous tissue → can lead to septicemia as infection

MCQ's.

1. An 86-year-old woman was admitted to hospital because of severe cellulitis secondary to an infected ingrown toenail. Knowing that thyroid disease is common in the elderly, a junior doctor requested thyroid function tests which came back as follows:

- **TSH 0.1 mU/l (0.3 – 4)**
- **fT4 8.0 pmol/l (9 – 26)**
- **fT3 2.0 pmol/l (3 - 8.8)**

Which of the following is the correct diagnosis in this case?

A) Severe hypopituitarism.
B) Sick euthyroid syndrome.
C) Thyrotoxicosis.
D) Hashimoto's thyroiditis.

2. A 26-year-old medical secretary consulted her GP because of excessive moisture in her skin which was causing her embarrassment at work. She was also concerned that her eyes seemed to have become more prominent and that she had lost weight, although her appetite was unchanged. On Examination, her doctor observed that her pulse was 92/min at rest and that she had a slightly enlarged thyroid gland. Investigations showed:

- TSH •0.01 mU/l (0.3 – 4)
- fT4 34 pmol/l (9 – 26)
- fT3 13 pmol/l (3 – 8.8)

An isotope scan of the thyroid showed an enlarged gland with uniformly increased uptake. Autoantibodies to thyroid peroxidase were present in the serum in high titres. Which of the following is the most likely diagnosis?

A) Severe anxiety.
B) Hypothyroidism.
C) Phaeochromocytoma.
D) Ophthalmic Graves's disease.

3. A 36-year-old woman was found to have a blood pressure of 190/110 mg/Hg by her GP at a routine health check. Laboratory tests showed that her serum potassium is 2.6 mmol/l (Ref: 3.6 – 5). She was given oral potassium supplement as well as thiazide diuretic for her hypertension. After three weeks, repeated serum potassium concentration was only 3.0 mmol/l.

- **The aldosterone: renin ratio was 2600 and plasma aldosterone : 1320 pmol/l (Ref: 100 - 450 pmol/l).**
- **ACT scan of the abdomen showed a small mass arising from the <u>left adrenal gland</u>.**

Which of the following is the most likely diagnosis?

A) Phaeochromocytoma.
B) Addison's disease.
C) Excess cortisol secondary to adrenal tumour.
D) Conn's syndrome.

4. A young man with type 1 diabetes mellitus attended the outpatient department for his regular follow-up and reported that he had been symptoms free since his last clinic attendance. He had been taught how to measure his own blood glucose concentration but did not do this, because he did not like pricking his finger to obtain capillary blood for testing. Investigations showed the following:

- **Blood glucose (2h after breakfast) was 18 mmol/l**
- **(Ref: 2.8 – 6)**
- **HBA1C: 6.5% (6.5 – 7).**

What is the explanation of the laboratory findings in this patient?

A) Diabetic ketoacidosis.
B) Poor diabetic control.
C) BMI should be measured to exclude morbid obesity.
D) Non-adherence to diet.

Answers: 1-B 2-D 3-D 4-B

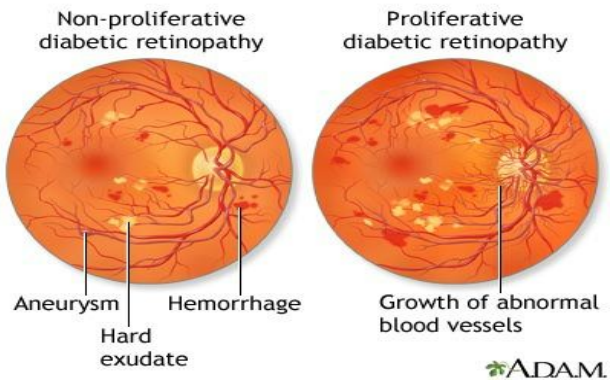
Explanation:

1. Euthyroid sick syndrome is low serum levels of thyroid hormones in clinically euthyroid patients with nonthyroidal systemic illness. Severe hypopituitarism is a wrong answer because hypopituitarism has severe clinical symptoms that weren't seen in the clinic.
2. Because of low TSH & high T3, T4.
3. In conn's syndrome there will be adenoma in the left adrenal gland (mostly) that secretes aldosterone. Aldosterone functions:
   a. increases excretion of potassium → hypokalemia.
   b. increase absorption of sodium → hypertension.

   Sometimes the adenoma can't be shown in the radiology
4. Question B is wrong because: HBA1C is used to check the patient's diabetic control over the previous 2-3 months. In this patient HBA1C was normal which indicates a good diabetic control.

Retinopathy is a complication of diabetes, in which stage it's considered irreversible?

Proliferative diabetic retinopathy (PDR).



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