001

Pages 1-25

M R C P (G L A S G O - U K) , M R C P - I R E L A N D for MRCP, part 1 & 2 3rd edition. 2022

Updated 2022

Third edition Notes & Notes

For MRCP By Dr. Yousif Abdallah Hamad Volume 1

Foreword

With the grace of the Almighty Allah, I have introduced the third edition of the popular book, the Notes & Notes for MRCP Part & 2. The MRCP exam requires a wide range of information, particular thinking, and question directed experience. This book is directed mainly at those who need comprehensive revision of the topics which commonly appear in the written MRCP exams. It will be helpful to go through these topics before you start solving the best of the five questions; it is also recommended to go quickly over this book in the last few weeks before the day of your exam. This new edition contains the new published guidelines.

I hope you will find the maximum benefits from this book to get through MRCP written exams.

To practice the best of five questions we advise you to join the best website for MRCP passonexam.com For any enquiry or comment, please do not hesitate to contact me.

“The mind is not a vessel to be filled, but a fire to be kindled.” — Plutarch.

March - 2022 Dr. Yousif Abdallah Hamad
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The 10 Golden Tips for MRCP written exams you will ever need

1. ```
   For MRCP, do not read hard; read smart.
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2. Three to six months is usually enough for preparation.
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3. Practice the best of the five questions as much as possible.
4. The few days before the exam date, stop revising questions and concentrate on your MRCP notes and top tips.
5. Remember, you are getting ideas and concepts from the questions.
6. Time factor in the exam room is the leading killer after poor preparation.
7. Manage your time wisely.
8. Read the end of the question first; if you can answer it without reading the whole scenario, it will save your time for the other tuff question (long scenario, .what is the action of imatinib?)
9. Take care for any single word in the question, e.g. (the initial test, the diagnostic test, the best test, the next step)
10. Practice, practice and practice.

Gestational diabetes mellitus (GDM).....

Pre-existing diabetes in pregnancy.....

Obesity: overview.....

Obesity: management (step-wise approach)

Lipid disorders: Overview.....

Familial Combined Hyperlipidaemia (type IIB)

Remnant hyperlipidaemia (type III).....

Familial hypertriglyceridaemia.....

Familial hypercholesterolaemia (FH).....

Secondary hypertriglyceridaemia.....

Hyperlipidaemia: management.....

Lipid-lowering agents.....

Statins.....

Fibrates.....

Ezetimibe.....

Nicotinic acid (niacin).....

Cholestyramine.....

Tangier disease.....

Abetalipoproteinemia.....

Gynaecomastia.....

Physiological changes during pregnancy – endocrine

Physiological effects of LH, FSH, and sex hormones

Dihydrotestosterone (DHT).....

Polycystic ovarian syndrome (PCOS)

Hirsutism.....

Hypertrichosis.....

Amenorrhoea.....

Premature ovarian failure.....

Menopause.....

Hormone replacement therapy (HRT).....

Selective Estrogen Receptor Modulators (SERMs)

Chapter 1 Endocrinolog & Metabolism Androgen insensitivity syndrome..... Disorders of sex hormones..... Menstrual cycle..... Hypogonadism..... Chapter 2 Pulmonology Lung anatomy..... Diaphragmatic paralysis (Phrenic nerve palsy) Lung physiology..... Oxygen Dissociation Curve..... Pulmonary function tests..... Obstructive vs. Restrictive lung diseases Transfer factor..... Transfer coefficient of carbon monoxide (KCO) Arterial Blood Gas (ABG)..... Chest x-ray..... Pleural calcification - Solitary pulmonary nodules Alveolar-arterial (A-a) oxygen gradient..... Finger clubbing..... Respiratory failure..... Bronchial Asthma..... Acute severe asthma..... Chronic Obstructive Pulmonary Disease(COPD) COPD: stable management..... Non-invasive ventilation (NIV)..... Invasive ventilation..... Long-term oxygen therapy (LTOT)..... Pulmonary embolism (PE)..... Recurrent pulmonary emboli..... Pulmonary embolism in pregnancy: diagnosis and management..... Fat embolism..... Community-acquired pneumonia (CAP) Klebsiella Pneumonia..... Legionella pneumonia (Legionnaires› disease) Mycoplasma pneumoniae..... Aspiration pneumonia..... Psittacosis (Chlamydia psittaci pneumonia) (Atypical pneumonia).....

Delayed puberty.....

Multiple endocrine neoplasia.....

Autoimmune polyendocrinopathy syndrome

(APS) (Polyglandular syndrome).....

Pseudomonas pneumonia.....

Hospital-acquired pneumonia (HAP).....

Pneumocystis Jirovecii pneumonia (PCP)

Coronavirus disease 2019 (COVID-19)

Aspergillosis: Types.....

Allergic bronchopulmonary aspergillosis (ABPA)

Aspergilloma.....

Invasive aspergillosis (IA).....

Alpha-1 antitrypsin (A1AT) deficiency.....

Acute respiratory distress syndrome (ARDS)

Altitude related disorders.....

Bronchiectasis.....

Cystic fibrosis (CF).....

Occupational asthma.....

Hypersensitivity pneumonitis (HP).....

Pneumoconiosis.....

Asbestos and the lung.....

Pleural mesothelioma.....

Silicosis.....

Berylliosis.....

Coal workers› pneumoconiosis (CWP).....

Primary ciliary dyskinesia (PCD).....

Kartagener›s syndrome.....

Lung cancer: General overview.....

Lung cancer: paraneoplastic features.....

Lung cancer: stepwise investigations.....

Performance status for patient of lung cancer and COPD

Hepatopulmonary syndrome (HPS).....

Pulmonary alveolar microlithiasis (PAM)

Pulmonary Alveolar Proteinosis (PAP)

Carbon monoxide poisoning.....

Smoking cessation.....

Menetrier›s disease.....

Dyspepsia.....

Malabsorption.....

Jejunal villous atrophy.....

Coeliac disease.....

Whipple›s disease.....

Tropical Sprue.....

Irritable bowel syndrome (IBS).....

Malnutrition.....

Lactose intolerance.....

Functional constipation.....

Energy from food.....

Protein losing enteropathy.....

Enteral feeding.....

Refeeding syndrome.....

Melanosis coli.....

Mesenteric ischaemia (ischaemic colitis)

Small bowel bacterial overgrowth syndrome (SBBOS)

Spontaneous bacterial peritonitis (SBP)

Liver function test.....

Liver biopsy.....

Acute liver failure.....

Ascites.....

Liver cirrhosis.....

Liver transplant.....

Portal hypertension.....

Hepatic encephalopathy.....

Hepatorenal syndrome (HRS).....

Wilson›s disease.....

Hyponatraemia in Patients with chronic liver disease

Alcohol.....

Alcohol induced hypoglycemia.....

Alcohol - drinking problems: management

Disulfiram.....

Alcoholic liver disease.....

The common abnormalities in chronic alcohol dependence

Alcoholic ketoacidosis.....

Non-alcoholic fatty liver disease (NAFLD)

(Non-alcoholic steatohepatitis (NASH)

Liver abscess.....

Hydatid cysts.....

Drug-induced liver disease.....

Budd-Chiari syndrome.....

Dysplastic colonic polyps.....

Peutz-Jeghers syndrome.....

Capsule endoscopy.....

Pseudomyxoma peritonei.....

Villous adenoma.....

Chapter 3 Gastroenterology Carcinoid tumours..... Diverticular disease..... Meckel›s diverticulum..... Intussusception..... Aorto-enteric fistulae (AEF)..... Angiodysplasia..... Anal fissure..... Anal fistula..... Crohn’s disease..... Crohn›s-like enterocolitis with mycophenolate mofetil Ulcerative colitis..... Inactive (quiescent) colitis..... Ulcerative colitis: colorectal cancer..... Inflammatory bowel disease: key differences IBD: histology..... Microscopic colitis (Collagenous colitis and Lymphocytic colitis)..... Collagenous colitis..... Lymphocytic colitis.....

Toxic megacolon (Toxic dilatation of the colon)

Radiation enteritis.....

Gastroenteritis.....

Diarrhoea.....

Biochemical abnormalities in persistent vomiting

Giardiasis.....

Clostridium perfringens.....

Bacillus cereus.....

Shigella.....

Yersinia enterocolitica.....

Gastrointestinal parasitic infections.....

Exotoxins and endotoxins.....

Pseudomembranous colitis (Clostridium difficile)

Gastroenteritis (GI).....

Scombrotoxin food poisoning.....

Perforated viscus.....

Endoscopy in patients on antiplatelet or

anticoagulant therapy.....

Third edition Notes & Notes

For MRCP part 1 & 11

Dr. Yousif Abdallah Hamad

Endocrinology

&

Metabolism

Updated 2022

By

Chapter 1

Endocrinolog & Metabolism

Pituitary gland conditions

Antidiuretic hormone (ADH) (Vasopressin)

Overview • Synthesized in the supraoptic nucleus of the hypothalamus. • Stored and secreted from the posterior pituitary gland • it contains arginine, so called arginine vasopressin (AVP) • Vasoconstrictive effects at higher levels • Increase of urea reabsorption in the collecting duct: increases the corticomedullary gradient and facilitates urine concentration • ACTH release

Functions

1. Antidiuresis: Act on V2 receptors → ↑↑ transcription and insertion of water (Aquaporin-2) channels into the apical membrane of distal convoluted tubule and collecting duct epithelial cells → ↑↑ water permeability → ↑ water reabsorption (retain water in the body) → excretion of more concentrated urine, i.e., antidiuresis.
2. Act on V1 receptors → Increase smooth muscle contraction (Vasoconstriction, uterine, GI and indirectly ↓coronary artery blood flow).
3. Increase release of von Willebrand & factor VIII., (Desmopressin used for haemophilia A & Von Willebrand disease).
4. Increase platelet aggregation, (prothrombotic at high dose).

Vasopressin receptors

Receptor
Second messenger
Location
Action
Agonist
♦Terlipressin ↑ splanchnic VC ↓ esophageal varices bleeding.
♦ Felypressin prolong the action of local anesthesia (safer than epinephrine in cardiac patients)
V3 or (V1b) V 1 or (V1a) ♦ vascular smooth muscle,
♦ platelet,
♦hepatocytes,
♦ myometrium G proteincoupled, phosphatidyli nositol/ calcium anterior pituitary gland G proteincoupled, phosphatidyli nositol/ calcium Renal
basolateral membrane of collecting duct,

V2

Adenylate cyclase/ cAMP Extra renal
(vascular endothelium)

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By Dr. Yousif Abdallah Hamad

♦vasoconstriction,
♦ myocardial hypertrophy,
♦ platelet aggregation,
♦ glycogenolysis,
♦ uterine contraction
releases ACTH, prolactin, endorphins

Anti-diuresis
(Insertion of aquaporin2 channels)
♦ Vasopressin (weak , short acting , given SC or IM) ♦ Desmopressin (more potent, long acting, given intra-nasally) Desmopressin (used for haemophilia A & Von Willebrand disease) ↑↑ release of von Willebrand & factor VIII.

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Factors increase secretion of vasopressin (stimulatory factors): • Increased osmolality of plasma (The main stimulus).

• Reduced extracellular volume, hypovolaemia, blood loss, and hypotension (less sensitive stimulus). • decreased thirst perception and reduced fluid intake.
• Advancing age
• Angiotensin II • Hypoglycemia • Increased pain • Opiates • Nicotine • Antineoplastic drugs •

Carbamazepine

Factors decreases secretion of vasopressin (inhibitory factors): • genetic conditions (Wolfram syndrome),
• tumours (Craniopharyngioma, Germinoma),
• inflammatory conditions (Sarcoidosis, Histiocytosis). • Ethanol (alcohol) ↓↓ calcium-dependent secretion of AVP
• Atrial natriuretic peptide, by inhibiting Angiotensin II-induced stimulation of AVP secretion • Cortisol

MRCPI-part-1- January 2018: H/O RTA + rapid pulse and low BP + low Na. • What is the most likely explanation for this patient's hyponatremia? Physiologic ADH (vasopressin) secretion Hyponatremia that develops after massive hemorrhage is likely dilutional. When baroreceptors detect decreases in effective arterial volume, such as after massive blood loss, they cause antidiuretic hormone (ADH) to be released from the pituitary gland to increase renal reabsorption of free water, diluting serum sodium levels and causing hyponatremia.
• What is the appropriate management of this patient? normal saline.
 Management of hypovolemic hyponatremia includes volume repletion with normal saline.
 Correction of hypovolemia removes the stimulus to release ADH, causing free water excretion by the kidneys, which leads to rapid correction of serum sodium levels.
 volume repletion with normal saline must occur at a slow rate, because rapid correction of hyponatremia can cause central pontine myelinolysis.

May 2016 exam -part-1: Which adaptive mechanism that prevent dying from dehydration?
 Increase of aquaporin-2 in the collecting duct. ADH (vasopressin) ↑ aquaporin-2 expression
 ↓ water excretion protect against dehydration

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 1

Endocrinolog & Metabolism

MRCPUK-part-1-january-2018: You are reviewing a patient with a history of cranial diabetes insipidus. He is passing 4–6 litres of urine per day. Expression of which channel is likely to be decreased most in the collecting duct? Aquaporin 2
 It is found in the apical membranes of collecting duct principal cells.
 Aquaporin 2 gene expression is increased by vasopressin, which leads to increased re-absorption of free water. Expression is therefore downregulated in response to cranial diabetes insipidus.

Syndrome of inappropriate ADH secretion (SIADH) (↑↑ ADH) Definition

• The syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a disorder of impaired water excretion caused by the inability to suppress the secretion of antidiuretic hormone (ADH) leading to euvolaemic, hypotonic hyponatraemia.

Causes Category Examples Malignancy • Small cell lung cancer (The most common cause) • Less common head and neck cancer, olfactory neuroblastoma Neurological • Stroke, subarachnoid haemorrhage, subdural haemorrhage • Meningitis/encephalitis/abscess Infections • Pneumonia, tuberculosis, symptomatic HIV,
Drugs • Sulfonylureas , Thiazides • SSRIs, tricyclics, mono-amine oxidase uptake inhibitors, phenothiazines • carbamazepine • vincristine , vinblastine • cyclophosphamide, chlorpropamide • omeprazole Other causes • Surgical procedures • porphyrias (SIADH is associated with acute intermittent porphyria)

Mechanisms • ↑↑ (ADH) ↑↑ water retention Euvolemic hyponatraemia (dilutional effects) low plasma osmolality + high urine osmolality with an elevated urine sodium (above 20 mmol/L) • Osmotic fluid shifts → Cerebral edema and ↑ intracranial pressure Features • Symptoms of hyponatremia (usually asymptomatic until the sodium level falls below 120 mmol/l)
 Mild: anorexia, nausea, vomiting, headache, muscle cramps (the earliest symptoms of acute hyponatremia are nausea and vomiting.) Moderate: muscle weakness, lethargy, confusion Severe: seizures, altered consciousness
• Normotensive • Symptoms of the underlying condition

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Diagnostic criteria: SIADH can only be diagnosed when the following criteria are satisfied:

1. The patient is clinically euvolaemic (no clinical evidence of fluid overload (oedema) or dehydration)
2. ↓ Plasma sodium (<134 mmol/l) → hypoosmolality (<280 mOsmol/kg)
3. ↑ Urine sodium (>20 mmol/l) and osmolality (>100 mOsmol/kg) → concentrated urine
4. Normal thyroid, adrenal, and renal function. It is important to note that normal thyroid is referring to primary hypothyroidism. Euthyroid sick syndrome does not preclude the diagnosis of SIADH.

Diagnostic criteria

Diagnostic criteria for SIADH Clinical and/or laboratory findings Hyponatremia ↓ Serum sodium < 135 mEq/L Hypoosmolality ↓ Serum osmolality < 275 mOsm/kg Concentrated urine ↑ Urine osmolality > 100 mOsm/kg Elevated urinary sodium ↑ Urine sodium concentration > 20 mEq/L Euvolemia No signs of hypovolemia No signs of hypervolemia (e.g. oedema) No alternative causes Normal thyroid, adrenal, and renal function → Other causes of euvolemic hypotonic hyponatremia have been excluded (e.g., hypothyroidism, hypercortisolism, AKI) It is important to note that normal thyroid is referring to primary hypothyroidism. Euthyroid sick syndrome does not preclude the diagnosis of SIADH.

Differential diagnosis • Cerebral salt wasting (CSW)
 hypovolaemia , hyponatraemia and grossly elevated urine sodium (>100) in patient with head injury. it treated with replacing fluid and sodium losses, whereas SIADH treated with fluid restriction

SIADH patients are usually euvolemic, normotensive, and have no edema. A hyponatremic patient with edema should raise suspicion of other conditions (e.g. congestive heart failure)

Notes & Notes for MRCP
By Dr. Yousif Abdallah Hamad Chapter 1

Endocrinolog & Metabolism

Management Restriction of water intake is the initial treatment of choice for hyponatraemic patients with SIADH who are not at imminent risk of seizures or coma. This precipitates a gradual rise in serum sodium, not greater than the recommended maximum of 8–10 mmol/day.

• Sever acute symptomatic hyponatraemia: (who present with neurologic abnormalities, e.g. seizures or ↓ conscious level). hypertonic (3%) saline given via continuous infusion Infusion of hypertonic (3%) saline is reserved for patients with acute severe life-threatening hyponatraemia, usually where sodium is less than 120 mmol/l and there are significant neurological features (i.e. seizures or GCS less than 11). correction must be done slowly to avoid precipitating central pontine myelinolysis The sodium serum levels may increase by a maximum of 10 mmol/L within 24 hours or 0.5 mmol/L per hour. • Mild acute OR chronic hyponatraemia: (Na+ ≥ 120 and NO neurological signs) 1st line → fluid restriction (the initial treatment of choice) Restriction of fluid to a daily intake of less than 800 mL/day. patients with subarachnoid hemorrhage are an exception since fluid restriction may promote cerebral vasospasm. 2nd line → demeclocycline it is a semi-synthetic tetracycline antibiotic →reduces the responsiveness of the collecting tubule cells to ADH (by inducing nephrogenic diabetes insipidus) 3rd line → ADH (vasopressin) receptor antagonists have been developed (ie. tolvaptan) Side effects → hepatotoxicity, excessive thirst

SIADH initial treatment: • If there is obvious precipitant (eg: drug) → stop the precipitant agent • where there is no obvious precipitant → fluid restriction → demeclocycline

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Diabetes insipidus (DI)

Diabetes insipidus is characterised by a high plasma osmolality and a low urine osmolality

Definition • The passage of large volumes (>3 L/24 hr) of dilute urine (< 300 mOsm/kg) due to deficiency of or insensitivity to antidiuretic hormone (ADH).

Types and mechanisms of DI

1. Cranial DI: caused by a deficiency of antidiuretic hormone (ADH) (the most common type)
2. Nephrogenic DI: caused by insensitivity to ADH (rare)
3. Primary polydipsia (dipsogenic DI): caused by a primary defect in osmoregulation of thirst.
4. Gestational DI: caused by degradation of vasopressin by a placental vasopressinase.

Causes of cranial DI • Primary
 Idiopathic (the most common primary cause) Hereditary (rare): Wolfram's syndrome (DIDMOAD) : association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness. • Secondary Brain tumors (especially craniopharyngioma) and cerebral metastasis Neurosurgery: usually after the removal of large adenomas Traumatic brain injury, pituitary bleeding, subarachnoid hemorrhage Pituitary ischemia (e.g., Sheehan syndrome, ischemic stroke) Infection (e.g., meningitis) Sarcoidosis Wolfram’s syndrome or the DIDMOAD syndrome is characterised by diabetes insipidus, diabetes mellitus, optic atrophy, and deafness

Causes of nephrogenic DI • Genetic: two forms:

1. vasopressin-2 receptor (V2 ADH) mutation
   the more common form, X linked (usually male are affected)
2. mutations in the aquaporin-2 gene → ↓water reabsorption in the distal tubule. less common form , autosomal recessive • Electrolytes:
   hypercalcaemia hypokalaemia → desensitization of renal tubules to (ADH) → ↑ water excretion
   • Drugs: the commonest precipitants tetracycline (demeclocycline) lithium → enters the principal cells of the collecting duct through the epithelial sodium channels (ENac) → inhibits signalling pathways that involve glycogen synthase kinase type 3 beta (GSK3beta) → dysfunction of aquaporin-2 water channel → nephrogenic DI.
   • Tubulo-interstitial disease: obstruction, sickle cell trait, pyelonephritis, Sjögren's syndrome. • Pregnancy (combined renal hyposensitivity to ADH, increased placental elimination of ADH, lowered thirst threshold and effect of fluid retention)

Hypokalaemia is a rare cause of polyuria and polydipsia

Nephrogenic DI is the most common adverse effect of lithium and occurs in up to 40% of patients

Features • Polyuria urine output is > 50 ml/kg per day (3000 ml for a 60-kg female). Nocturia → Restless sleep, daytime sleepiness (In the absence of nocturia, diabetes insipidus is very unlikely) • Polydipsia

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By Dr. Yousif Abdallah Hamad Chapter 1

Endocrinolog & Metabolism

Diagnosis
In suspected DI the most appropriate next investigation is → Urine and plasma osmolality (non-invasive first step)

• High plasma osmolality plasma osmolality >305 mOsmol/kg serum [Na] >145 mmol/L • Low urine osmolality urine osmolality <200 mOsm/kg urinary [Na] 20-60 mmol/L urinary specific gravity <1.005. • Water deprivation test with response to desmopressin (The patient is deprived of fluids for up to eight hours or 5% loss of body weight, following which desmopressin (DDAVP®) 2 micrograms (IM) is given).

 CDI → ↓ urine osmolality and ↑ serum osmolality CORRECTED by Desmopressin administration (plasma osmolality normalizes and urine osmolality rises). NDI → low urine osmolality and elevated serum osmolality, with no significant response to desmopressin. • CT scan or MRI of the head: If CDI is diagnosed, to rule out brain tumors

Management • Central DI Mild CDI (urine output 3-4 litres/24 hours) → increase oral water intake.
 oral or nasogastric water is the replacement fluid of choice as this route provides a good buffer against rapid changes in serum sodium.

 If the urine output continues to be greater than 250 ml/hr → Desmopressin (Synthetic ADH) is the drug of choice.

• Nephrogenic DI → correct the underlying cause (e.g. stop the responsible drug) Thiazide diuretic (eg, hydrochlorothiazide), amiloride (K- sparing diuretic) → act on Distal Convoluted Tubule and inhibit the NaCl cotransporter and thus exaggerate the hypovolemia and increase an already activated renin–angiotensin–aldosterone system (RAAS) further. This mechanism stimulates proximal tubule sodium and water reabsorption resulting in less volume delivery to the collecting tubules where ADH work. NSAIDs (indomethacin) → inhibit prostaglandin synthesis, which has antagonistic effects on ADH. Amiloride is the drug of choice for lithium – induced nephrogenic DI → blocks the epithelial sodium channel (ENac) in the collecting duct where lithium enter and causes DI.

Rate of hypernatraemia correction • Symptomatic patients with acute hypernatraemia (developed within 48h) → 5mmol/L in the first hour (or until symptoms improve) and is limited to 10mmol/L per 24h. • No or mild symptoms → the rate of correction should not exceeding 0.5mmol/L/h and is limited to 10mmol/L/24h.

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Fluid status in DI • Total body water: decrease • Extracellular fluid: increase • Intracellular fluid: decrease DI → losing hypotonic fluid in the urine → ↑ osmolarity of the extracellular fluid → water will flow out of the intracellular compartment and into the extracellular compartment → ↑extracellular fluid volume and ↓intracellular fluid volume.

Which part of the nephron is most affected in diabetes insipidus? Cortical and medullary collecting tubules

If there is hypovolaemic hypernatraemia ((hypotension, tachycardia, poor skin turgor)): The first step is to restore volume with isotonic fluids (0.9% saline).

Water deprivation test

Overview
• The diagnostic test to confirm DI is a water deprivation test. • The goal of water restriction is to

raise the plasma sodium to at least 145 mEq/L and plasma osmolality to 295 mOsmol/kg to stimulate enough ADH release to concentrate urine in normal subjects. If water restriction does not raise the Na and osmolality to this level, hypertonic saline infusion may be necessary.
• Normal plasma osmolality is 285-305 mosmol/kg. • The normal 24-hour urine osmolality is, on average, 500-800 mOsm/kg of water.
Method • Prevent patient drinking water (for a period of 8 h or until 5% of body weight is lost).
• Ask patient to empty bladder • Patients should be weighed hourly.
• Test urine volume and osmolality every hour • Test sodium and plasma osmolality every two hours • Water deprivation continues until one of the following occurs:

1. Urine osmolality rises and reaches a normal value (> 600 mOsmol/kg) → DI ruled out and primary polydipsia confirmed Where urine osmolality reaches levels above 600 mOsmol/kg without desmopressin, then the diagnosis is primary polydipsia.
2. No change in urine osmolality despite a rising plasma osmolality (> 290 mOsmol/kg)
3. Plasma osmolality > 295–300 mOsmol/kg or sodium ≥ 145 meq/L • In the latter two situations → administer desmopressin (a synthetic ADH analog) 2 µg intramuscular Monitor urine osmolality testing every 30 minutes for 2 hours In CDI: Urine osmolality rises (> 600) after desmopressin administration (renal ADH receptors are intact). In NDI: Urine osmolality remains low after desmopressin administration (defective renal ADH receptors).

Chapter 1

Endocrinolog & Metabolism

Classification of causes of diabetes insipidus on basis of water deprivation and DDAVP® response

Primary polydipsia
(psychogenic polydipsia) • Hyponatremia (< 137 meq/L) • Plasma osmolality: low- normal (255–280 mOsmol/kg) • Very low urine osmolality (< 250 mOsmol/kg) Lab findings on presentation Water deprivation test results • Plasma osmolality: normal (275– 290 mOsmol/kg) • Urine osmolality: rises, reaches normal value (> 600 mOsmol/kg) This result shows that both ADH release and effect are intact. Desmopressin administration results • Water deprivation test results confirm diagnosis; no need to administer desmopressin

Classification of causes of diabetes insipidus on basis of water deprivation and DDAVP® response Urine osmolality after fluid Urine osmolality after DDAVP® (mOsm/kg) Likely diagnosis deprivation (mOsm/kg) <300

> 800 Cranial DI <300 <300 Nephrogenic DI 800 800 Primary/psychogenic polydipsia <300 800 Partial cranial DI or nephrogenic DI or PP or diuretic abuse

A dramatic improvement in the ability of the kidneys to concentrate urine following the administration of DDAVP points towards a diagnosis of cranial diabetes insipidus

Differentiate psychogenic polydipsia from CDI and NDI: • Patients with this disorder ingest and excrete up to 6L of fluid/day and are often emotionally disturbed.
• Unlike patients with CDI and NDI, they do not have nocturia, nor does increased thirst wake them at night. • Patients with acute psychogenic polydipsia can concentrate their urine during a water deprivation test but chronic water intake diminishes medullary tonicity in the kidney.
• Patients with long-standing polydipsia are not able to concentrate their urine to maximal levels during water deprivation, a response similar to that of patients with partial central diabetes insipidus.
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CDI NDI • Mild hypernatremia (> 150 mEq/L) • High-normal plasma osmolality(280–290 mOsmol/kg) or slightly elevated • Low urine osmolality Partial DI: 300–500 mOsmol/kg Complete DI: < 300 mOsmol/kg • Plasma osmolality: rises (> 290 mOsmol/kg)
• Urine osmolality: no change • Plasma osmolality: normalizes (275– 290 mOsmol/kg) • Urine osmolality
rises • Plasma
osmolality remains elevated • Urine osmolality remains low

• However, unlike central diabetes insipidus, patients of psychogenic polydipsia show no response to exogenous ADH after water deprivation. This response resembles nephrogenic diabetes insipidus, but ADH levels are low in psychogenic polydipsia and high in nephrogenic polydipsia.

Polyuria

Definition
• defined as a urine output exceeding 3 L/day

Causes Common (>1 in 10) Infrequent (1 in 100)

• diuretics, caffeine & alcohol • diabetes mellitus • lithium • heart failure • hypercalcaemia • hyperthyroidism

Thiazide diuretic abuse • polyuria and polydipsia of recent onset + high calcium, glucose and hypokalaemia, with an elevated bicarbonate. ↑Serum Osmolality > 300

Hyponatraemia (serum sodium less than 135 mEq/L).

Prevalence • Occurs in up to 30% of hospitalised patients

Classifications • based on severity: Mild hyponatraemia : serum sodium between 130 and 135 mmol/l
 Moderate hyponatraemia: serum sodium between 125 and 129 mmol/l
 Profound hyponatraemia: serum sodium <125 mmol/l • based on time of development: Acute hyponatraemia: hyponatraemia that is documented to exist < 48 h. Chronic hyponatraemia:

hyponatraemia that is documented to exist ≥ 48 h. If hyponatraemia cannot be classified, we consider it being chronic

Mechanisms of causes

1. water excess
2. sodium depletion
3. Pseudohyponatraemia: (isotonic hyponatraemia) Causes Hyperglycaemia hyperlipidaemia (increase in serum volume)
   - hyperproteinemia (e.g. myeloma)
   - taking blood from a drip arm.
   - exclude hyperglycaemic hyponatraemia by measuring the corrected serum Na+ Notes & Notes for MRCP
     By Dr. Yousif Abdallah Hamad

Rare (1 in 1000)

Very rare (<1 in 10 000)

• chronic renal failure • primary polydipsia • hypokalaemia • diabetes insipidus

Chapter 1

Endocrinolog & Metabolism

 adding 2.4 mmol/l to the measured serum sodium for every 5.5 mmol/l incremental rise in serum glucose concentration above a standard serum glucose concentration of 5.5 mmol/l. corrected Na+ = measured Na+ + 2.4 x (serum glucose mmol – 5.5/5.5mmol) Non-hypotonic hyponatraemia does not cause brain oedema and is managed differently from hypotonic hyponatraemia.

Causes of hyponatraemia Pseudohyponatraemia is characterised by a normal measured serum osmolarity, however the calculated osmolarity (based on an erroneously low plasma sodium result) is reduced. This results in a raised osmolar gap Urinary sodium > 20 mmol/l Urinary sodium < 20 mmol/l Sodium depletion, renal Patient often loss (patient often euvolaemic hypovolaemic) • diuretics • diuretic stage of renal failure • Addison's • SIADH (urine osmolality > 500 mmol/kg) • hypothyroidism

• secondary hyperaldosteronism: heart failure, cirrhosis • reduced GFR: renal failure • IV dextrose, • psychogenic polydipsia

Features
• Fatigue, Muscle weakness • Gait disturbance, Falls • Cerebral oedema Disorientation, Seizures

Investigations • Urinary sodium and osmolarity levels aid making a diagnosis. urinary sodium Reduced urinary sodium excretion [less than 30 mmol/l] may indicate total body sodium depletion even if plasma sodium levels are normal. may be misleading in the presence of renal

impairment or diuretic therapy.

Notes & Notes for MRCP
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Sodium depletion, Water excess (patient often hypervolaemic and extra-renal loss (hypovolaemic) oedematous) • diarrhoea, vomiting, sweating • burns, adenoma of rectum

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Management
• ascertain volume status as this will determine management.
 Hypovolaemic hyponatraemia Diagnosis may supported by an elevated urea suggesting dehydration.
 rehydration with sodium chloride 0.9% or a balanced crystalloid (Hartmann's) avoid rapid Na correction to reduce the risk of central pontine myelinolysis. The rate of Na correction should not exceed 8 mEq/L per day. Euvolaemic hyponatraemia check urine and serum osmolality. Does the patient meet the criteria for SIADH? treat the underlying cause where possible in SIADH fluid restriction (500-750mls/day) monitor fluid balance and perform daily weights consider demeclocycline or tolvaptan (under specialist supervision). Both inhibit the action of antidiuretic hormone. Hypervolaemic hyponatraemia fluid and salt restriction consider diuretics treat the underlying cause (e.g. cardiac failure)

Notes & Notes for MRCP
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Endocrinolog & Metabolism

Hyponatraemia: correction

Acute hyponatraemia
• predisposing factors to acute hyponatraemia: Over consumption of fluids,
 Post-operative hyponatraemia is not uncommon and is likely to be due to a combination of SIADH which develops in the post-op period and the infusion of inappropriate IVIs. prolonged race duration and inadequate training
• Pathophysiology When hyponatraemia develops over a short duration the ability of the brain to adapt is exceeded and cerebral oedema can result which may lead to confusion, seizures and coma. As a result, patients may die from brain herniation. • Features hyponatraemic encephalopathy which is life threatening and presented with a fit. • Treatment of Hyponatraemia with severe symptoms Hypertonic saline (3%) boluses are the most appropriate treatment to improve neurological status in such patients. 150mls of 3% hypertonic saline over 20 mins check the serum sodium after 20 min while repeating an infusion of 150 ml 3% hypertonic saline for the next 20 min. repeat therapeutic twice or until a target of 5 mmol/l increase in serum sodium is achieved The target sodium by which one should elevate the sodium is 5 mmol/l over the first hour. limit the increase in serum sodium to a total of 10 mmol/l during the first 24 h and an additional 8 mmol/l during every 24 h thereafter until the serum sodium concentration reaches

130 mmol/l Decompressive craniotomy would help alleviate raised intracranial pressure due to cerebral oedema however is not an appropriate first line treatment.

Hypopituitarism

Definition • Deficiency of one or more anterior pituitary hormones. GH deficiency → growth retardation (during childhood), ↓ bone density, muscle atrophy, hypercholesterolemia Prolactin deficiency → lactation failure following delivery
 FSH/LH deficiency → hypogonadotropic hypogonadism (secondary hypogonadism) TSH deficiency → secondary hypothyroidism ACTH deficiency → secondary adrenal insufficiency
• Hypopituitarism becomes symptomatic when more than 80% of pituitary cells are damaged.

Acute hyponatraemia is that which occurs within a duration of 48 hours.

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