Hypernatremia

A) Net water loss

Hypotonic fluid

a- Renal losses :
- Loop diuretics
- Osmotic dieresis
- Postobstructive dieresis
- Intrinsic renal disease

b- Non-renal losses:
- Vomiting
- NG suctioning
- Enterocutaneous fistula
- Burns
- Excessive sweating

Pure water

- **Central DI:**
  - Low ADH secretion.
  - Idiopathic 50% / head trauma/ destructive disea.
- **Nephrogenic DI:**
  - Unresponsiveness of renal tubules to ADH.
  - Acquired : Chronic Lithium use (most)/ Hypercalcemia/UTI (pyelo)
  - Congenital

Diagnosis:

- Urine: ↓ SG/Osmolality.
- P.osmolality:

Normal: 250 to 290 mOsm/kg

DI: 280 to 310 mOsm/kg

- A water deprivation test :
  - Withhold fluids, and measure urine osmolality every hour
  - When urine osmolality is stable (<30 mOsm/kg hourly increase for 3 hours), inject 2 g desmopressin S.C. Measure urine osmolality 1 h later :

	Urine osmo	response to ADH
Normal	+	-
C-DI	-	+
N-DI	-	-

B) Hypertonic sodium gain

Primary hyperaldosteronism

- ↑ aldosterone secretion from adrenal gland.
- **Causes:**
  - * functioning adenoma→ **"Conn Syndrome"**
  - * Bilaterral Adrenal Hyperplasia
- **C/P**
  - * ↑ Na & Water → **Hypertension**
  - * ↑K & H ions → **Hypokalemia & M.Alkalosis**
  - \+ 1) Polydipsia, nocturnal polyuria (due to hypokalemia) 2) Absence of peripheral edema
- **Diagnosis:**
  - * Screening:

Plasma:↑ aldosterone /↓ rennin/**A:R ratio>30**

  - * Confirmation: with either:
    - **1) Saline infusion test:**
      - Infusion of saline will decrease aldosterone levels in normal patients
    - **2) Oral Sodium Loading**
  - * Diagnose cause:

1**) Adrenal venous sampling**

↑ aldosterone level on one side indicates an adenoma.

↑ aldosterone on both sides indicate bilateral hyperplasia.

2) Imaging tests
- **Treatment:**

1. For adenoma— adrenalectomy.
2. For bilateral hyperplasia
   a. Spironolactone ↓ action of aldosterone.
   b. Surgery is not indicated.

Cushing syndrome

- ↑ cortisol level :

A) Iatrogenic : exogenous steroids (most common)

B) Non-iatrogenic:
- * ACTH independent → from adrenal gland (1ry)
- * ACTH dependent→ 2ry :
  - -- ↑ACTH From pituitary: "Cushing's disease"
  - -- Etopic ACTH production : SSC of lung
- **C/P**

-Changes in appearance: central obesity, hirsutism,moon facies, "buffalo hump," purple striae on abdomen, acne/

- Diabetes ,Hypertension
- Hypogonadism, Masculinization in females, proximal muscle wasting and weakness, Psychiatric disturbances
- **Diagnosis:**
  - Screening:
    - **1) low-dose dexamethasone suppression test**
      - * If the serum cortisol is <5 → No Cushing.
      - * If the serum cortisol is >5 → Cusing syndrome
    - **2) 24-hour urinary free cortisol level**
  - ACTH level:
    - * If low→ 1ry Cushing(adenoma/or hyperplasia)
    - * If high→ 2ry (pituitary /or ectopic production):

to differentiate between pituitary & ectopic ACTH:

a) High dose dexa suppression test :
In Pituitary →decrease in cortisol > 50%
In ectopic → No suppression occur.

b) CRH stimulation test.

Hyponatremia

1- Euvolemic (Urine Na > 20 → patient not Hypovolemic)

Urine Osmolality < 100 : **Psychogenic polydepsia**

Urine Osmolality > 100 : **the urine is inappropriately concentrated :**

SIADH

Diagnostic test: ↑ Urine osmolality > 100 / ↑ urine Na > 40
↓ Plasma osmolality < 280

The most accurate test is a high ADH level.

Causes

CNS
-Head trauma (SAH)
-Tumor

Sub Arachnoid Hemorrhage "SAH" :
Causes: 1st trauma / 2nd berry aneurysm
Sudden severe headache (worst in my life)
+ signs of meningeal irritation + **Fluctuating LOC**
do CT scan before LP (↑ ICP, RBCs, xanthochromia)
Once confirmed → Four-vessel angiography

Plumonary
- **Fever,** malaise , weight loss
- **cough, dyspnea,**
- **Polyarthritis**

TTT:
Systemic Steroids

Sarcoidosis : Non-caseating granulomas

C/P : GRUELING	Investigations
Granulomas a**R**thritis **U**veitis **E**rythema nodosum **L**ymphadenopathy **I**nterstitial fibrosis **N**egative TB test **G**ammaglobulinemia	**CXR:** Bilateral hilar lymphadenopathy alone **Biopsy:** noncaseating granulomas **PFTs:** ↓ lung volumes (restrictive pattern)

Brain : cranial nerve defects (Facial palsy)
Heart : arrhythmias/ restrictive cardiomyopathy

3↑: **serum ACE levels** / **Hypercalcemia,** ALP (liver).
1 ↓ lymphopenia.

Paraneoplastic syndrome

Small cell lung cancer (SCLC)
Cigarette exposure + Central location.

Drugs

SSRis, tricyclic antidepressants/ vincristine, cyclophosphamide/ sulfonylureas

Adrenal insufficiency

-I feel Tired (Weakness, fatigue)
-because I'm "anorexic, vomiting , lost weight" & **hypotensive**
- Hyperpigmentation

Types

1ry	2ry
Mostly by : **Autoimmune destruction (Addison's disease)** **Others:** **-TB → CT shows: calcification** **-Metastasis** **-Hemorr. → acute + blood in CT** **-Adrenoluckodystrophy → VLCFA + enlarged glands in CT**	↓ ACTH by the pituitary, by: **MRI +ve → tumor** **MRI –ve → Long-term Steroids use**

Hyponatremia + eosinophilia + Hypercalcemia (1/3)

No aldosterone :	ACTH independent
• **Hyperkalemia**	• **Normal**
TTT **Glucocorticoid+mineralocorticoid**	**TTT** **Glucocorticoid**

In adrenal crisis : 4 S
Salt: 0.9% saline **S**teroids: IV hydrocortisone 100 mg q 8 hours
Support **S**earch for the underlying illness

Diagnosis : **1- Synthetic ACTH stimulation test**:
Cosyntropin → plasma cortisol level < 20 ug/dl
2- **Insulin tolerance test**.

Hypothyroidism

-I feel Tired (Weakness, fatigue)
- I'm " Constipated , gain weight " / braycardiac
- cold intolerance / dry , cold , puffy skin.

Causes of 1ry hypothyroidism

1- Hashimoto's thyroiditis :
- Hashitoxicosis → followed by hypothyroidism
- Lab: +ve Anti-TPO antibodies / antimicrosomal antibodies
- Biopsy: lymphocytic infiltration.

2- hypothyroid phase of thyroiditis :
- Subacute & radiation-induced forms → **tender thyroid**
- Diganosis: **↓ uptake on RAIU during thyrotoxic phase**

3- Iatrogenic factors :
a- Radioactive thyroid ablation or excision
b- Infiltrative disease
c- Drugs: **Lithium / Amiodarone**

β-blockers for **hyperthyroidism**/levothyroxine for **hypothyroidism**.
NSAIDs or oral steroids in severe cases for : **Subacute thyroiditis.**

Myxedema coma : severe hypothyroidism with: (Mortality 60%.)
↓ mental status + hypothermia + other parasympathetics
TTT 1- IV levothyroxine
2- IV hydrocortisone (if adrenal insufficiency has not been excluded)

Diagnosis :
1ry : ↑ TSH / ↓ T4 & T3 (T3 to lesser extent)
2ry & 3ry : Normal or ↓ TSH / ↓ T4 & T3

2- Hypovolemic

Urine Na < 20 : **1- Vomiting 2- Diarrhea 3- Nasogastric tube 4- Sequestration of fluid in burns , ilues , Traumatized muscle , pancreatitis**

Urine Na > 20 :

1- Diuretics

Loop	Water loss	Metabolic alkalosis		↓ Ca^{2+}	↓ K^{+},		sulfa allergy	**Ototoxicity**
Thiazide	Water loss,	Metabolic alkalosis	↓ Na^{+}	↑ Ca^{2+}	↓ K^{+},	↑glucose /↑Uric acid	sulfa allergy	Pancreatitis

2- Mineralcorticoid deficiency

1- Na^{+} loss →with **Hyponatremia, hypovolemia, hypotension**
2- Impaired secretion of both K^{+} and H^{+} in the renal tubules → **Hyperkalemia & metabolic acidosis**

3- Hypervolemic

Urine Na > 20 : **1- Acute & chronic renal failure**

ARF	Causes	Urine osmolality	Urine Na	FE_{Na}	FE_{UREA}	BUN/creatinine
Pre-renal	Hypoperfusion in : heart failure / liver failure / sepsis / burns / bilateral renal artery stenosis	**>500** : dehydration release ADH leading to increases water absorption	**<20**	**<1 %**	**<= 35 %**	**>20 : 1**
Renal	Acute tubular necrosis (ATN) "most common" / Allergic interstitial nephritis (AIN); Glomerulonephritis; / Nephrotoxin exposure (including myoglobin from rhabdomyolysis);	**<300** : Similar in osmolality to blood (300 mOsm/L). This is called isosthenuria	**>20**	**>1 %**	**> 50 %**	**< 20 : 1 (about 10:1)**
Post-renal	Obstruction 2ry to : benign prostatic hypertrophy (BPH) / bladder & pelvic tumors / calculi	**<350**	**>40**	**>4 %**		**20 : 1**

- **Hyaline casts** - Normal, BUT ↑ amount suggests dehydration – Prerenal
- **Red cell casts, dysmorphic red cells** – Glomerulonephritis – Intrinsic
- **Granular casts "muddy-brown cast" , tubular cells**– Acute Tubular Necrosis – Intrinsic
- **White cells, eosinophils** – Acute (Allergic) interstitial nephritis – Intrinsic (**Wright & Hansel stains** detect eosinophils in urine) */ NO eosinophils in NSAID*
- **White cells, white cell casts** – Pyelonephritis – Postrenal (**WBC with -ve culture: TB)**

***Indications for urgent dialysis*— AEIOU**
Acidosis
Electrolyte abnormalities (hyperkalemia)
Overload (fluid).
Uremic symptoms (**pericarditis, encephalopathy**, bleeding, nausea, pruritus, myoclonus).

Urine Na < 20 : **Causes of generalized edema :**

Nephrotic syndrome

Criteria of diagnosis (4) : 1- Proteinuria (≥ 3.5 g/day) 2- Hypoalbuminemia (< 3 g/dL) 3- Hyperlipidemia (>250 mg/dl) 4- Generalized edema

Minimal change Disease	- Most common cause in children - 1ry idiopathic - 2ry causes : NSAIDs	Tendency toward : - Infection - Thrombotic events	LM: Normal EM: fusion of epithelial foot processes	TTT: Steroids Excellent prognosis
Focal segmental glomerulosclerosis	- Idiopathic - IV drug use - HIV infection - Obesity	Young black male with uncontrolled hypertension	LM: sclerosis in capillary tufts + microscopic hematuria	- Prednisone - Cytotoxic therapy
Membranous nepthropathy	2ry causes : - Solid tumor malignancies. - Immune complex disease	- Mostly in Caucasian adults - Associated with : HBV / syphilis / malaria / gold	"Spike & dome appearance" Due to granular deposits of : IgG & C3 at the basement membrane	- Prednisone - Cytotoxic therapy
Membranoproliferative nephropathy	Can also be nephritic syndrome. **Slow progression to renal failure.**	- Type I is associated with : HCV / cryoglobulinemia / lupus / subacute bacterial endocarditis.	- **"Tram-track,"** double-layered basement membrane. - Type I : subendothelial deposits + mesangial deposits; - Type II :	- Prednisone - Cytotoxic therapy
Diabetic nephropathy	Two forms: 1- Diffuse hyalinization 2- Nodular glomerulosclerosis (Kimmelstiel-Wilson lesions)	Long-standing, poorly controlled DM with evidence of retinopathy or neuropathy.	- Thickened GBM - ↑ mesangial matrix	- Control of diabetes - ACEIs for type1DM - ARBS for type2DM
Renal amyloidosis	1ry : plasma cell dyscrasia 2ry: infectious / inflammatory	May Associations with : 1- Multiple myeloma 2- RA	- Fat pad biopsy / Seen with Congo red stain - Apple-green birefringence by polarized light	- Prednisone - Melphalan

Lupus nephritis		
I	• No renal involvement visible by histopathology	
II	• Mesangial disease with focal segmental glomerular pattern	• Tx not typically required for kidney involvement
III	• Focal proliferative disease	• Tx = aggressive prednisone ± cyclophosphamide
IV	• Diffuse proliferative disease, (Classic LM:- wire-loop abnormality)	• Tx = prednisone + cyclophosphamide, transplant may be required
V	• Membranous disease, indistinguishable from other 1 ry MGNs	• Tx = consider prednisone, may not be required

Cirrhosis

Abnormal LFTs: ↓ **albumin,** ↑ **PT/PTT,** ↑ **bilirubin. /** Anemia or thrombocytopenia (2ry to hypersplenism).

1- Chronic hepatitis: HCV / HBV → Search for serological markers.

HBV : HBsAg → found on the surface of HBV; continued presence indicates carrier state.
HBsAb → **provides immunity** to HBV.
HBcAg → associated with core of HBV.
HBcAb → during **window period.** IgM HBcAb is an indicator of recent disease.
HBeAg → antigenic determinant in the HBV core. An important indicator of transmissibility. (**BE**ware!)
HBeAb → indicates low transmissibility

2- Biliary tract diseases :

a- **1ry biliary cirrhosis :** the most accurate test is "liver biopsy" / TTT: ursodeoxycholic acid
- **Middle aged Femal > male** with RA, Sjögren syndrome, Scleroderma + progressive **jaundice, pruritus, fatigue**
- Lab: ↑ **ALP+GGTP**, **Normal bilirubin BUT elevated in advaced** , *most specific: +ve **antimitochondrial antibody.***

b- **1ry sclerosing cholangitis: the most accurate test is "ERCP"/ TTT:**cholestyramine or ursodeoxycholic acid
- **Yong male > female** with **IBD** (ulcerative colitis) + progressive **jaundice, pruritus, fatigue**
- Lab: ↑ **ALP+GGTP+bilirubin** / ERCP : **multiple bile duct strictures** / Liver biopsy:periductal sclerosis ("onion skinning")

3- Budd-Chiari syndrome :
- Hypercoagulability → hepatic vein thrombosis → acute onset of abdominal pain, jaundice → cirrhosis (Dx:RUQ US)

3- Wilson's Disease : autosomal-recessive defect on Chr. 13. / Age < 30 years of age : **ABCD**- **A**sterixis **/ B**asal ganglia deterioration **C**eruloplasmin ↓ , **C**opper ↑ **C**irrhosis , **C**arcinoma , **C**horeiform movements **/ D**ementia

4- Alcohol Liver cirrhosis :

5- Alpha 1-Antitrypsin Deficiency

6- Hemochromatosis

Congestive heart failure

Systolic Dysfunction	Diastolic Dysfunction
Impaired contractility → decrease in **EF**	Impaired ventricular filling during diastole (either: ↓ relaxation or ↑ stiffness or both)
1- HTN , resulting in cardiomyopathy 2- Post-MI (IHD) 3- Valvular heart disease 4- Myocarditis (postviral)	1- HTN: Most common cause. 2- Valvular: AS , MS , AR 3- Restrictive cardiomyopathy (e.g.,amyloidosis, sarcoidosis, hemochromatosis)
Symptoms: Dyspnea, orthopnea, Paroxysmal nocturnal dyspnea, Nocturnal cough (nonproductive) **Signs:** Displaced PMI, Pathologic S3, S4 gallop , Crackles/rales at lung bases, ↑ intensity P2 indicates pulmonary HTN (heard over left upper sternal border).	**Symptoms & signs :** Peripheral pitting edema,JVD, Ascites, Nocturia Hepatomegaly/hepatojugular reflux, Right ventricular heave. ***left-sided heart failure will always lead to right-sided heart failure and vice versa***
- Diuretics -Digitalis Drugs that lower mortality : 1- ACEIs / ARBs 2- Spironolactone 3- B-Blockers 4-Hydralazine, plus nitrate	**Patients are treated symptomatically:** (**NO** medications have proven mortality benefit) 1- ACEIs / ARBs 2- B-Blockers. 3- Diuretics **Digoxin & spironolactone should NOT be used!**