2020 內專複習班-補充

Nephrology

F1 王弘偉

單元 \ 題數	108	107
腎絲球疾病 ▲	3	2
慢性腎臟病 ▲	3	6
急性腎損傷 ▲	4	2
透析治療	1	1
酸鹼平衡	0	2
水分及離子平衡	2	2
高血壓相關	2	2
腎臟血管	0	0
感染	0	0
腎移植	2	0
藥物	2	1
其他 ▲	3	4
總題數	22	22

CA(I)AKI

- Contrast associated AKI: 在contrast使用後48小時內發生任何AKI都算,不一定具有因果關係
- Contrast induced AKI:contrast和AKI具有因果關係
- Risk factor: CKD, DM, albminuria, HF, age, increased contrast volume
- Prophylaxis (for eGFR<30ml/min/1.73m2): NaCl (500cc before/after, 1-3cc/kg/hr), 有risk的病人停用ACEi/ARB
- 不建議:prophylactic洗腎, NAC!

Diabetic nephropathy

- Albuminuria (>300mg/24hrs) + diabetic retinopathy + no evidence of other renal disease
- 第一型DM要10年才會進展成腎病變;第二型DM可能診斷時就已經有腎病變
- Gene: ACE DD genotype惡化風險高
- Pathology: GBM/TBM變厚,mesangial/interstitial expansion, arteriolar hyalinosis, Kinnelstiel-Wilson nodules
- Treatment: 控制三高,蛋白限制

Fibrillary GN; Immunotactoid GN

- Fibrillary: fibrils with 16-24nm, 分布散亂, in adults, 跟惡性腫瘤,monoclonal gammopathy, 自體免疫疾病有關, 病理: IgG, C3, kappa and lumda chains, polyclonal
- Immunotactoid: larger hollow microtubules with 30-50nm, 平行分布, older, less progressive course, 跟lympho-proliferative disease有關, IgG, kappa or lumda chains, monoclonal

Light chain disease vs. myeloma cast nephropathy

- Monoclonal Ig deposition disease: light-chain (LCDD), combined light and heavy chain (LHCDD), heavy-chain disease (HCDD)
- LCDD: most common, 80% kappa light chains (主要constant region), VkIV subgroup, patho: glomerulosclerosis, complement stain: negative, dense material along GBM
- HCDD: deletion of CH1 of heavy chain, positive for heavy chain gamma

- Cast nephropathy: Bence Jones protein+Tamm-Horsfall glycoprotein(Henle粗上升支)形成cast,塞住distal tubule

Analgesic nephropathy

- Aspirin/antipyrine+phenacetin/Paracetamol; salicylamide+caffeine/codeine
- Combined analgesic: 6 tablets/qd > 3 years
- More frequently in women
- Suppress prostaglandins, compromise renal blood flow
- Flank pain, hematuria, anemia, urinary tract malignancy ?
- Chronic interstitial nephritis, papillary calcification/necrosis

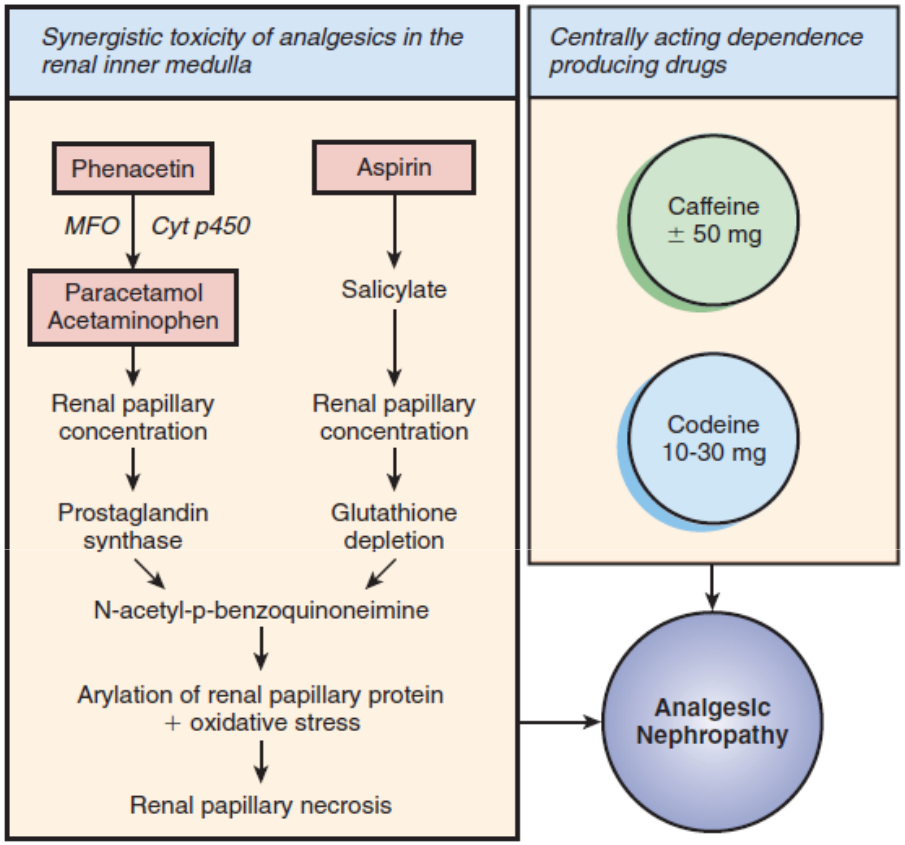

Figure 36.2 Synergistic toxicity of analgesics in the inner medulla and centrally acting dependence-producing drugs lead to analgesic nephropathy. Acetaminophen undergoes oxidative metabolism by prostaglandin H synthase to a reactive quinone imine that is conjugated to glutathione. If acetaminophen is present alone, sufficient glutathione is generated in the papillae to detoxify the reactive intermediate. If the acetaminophen is ingested with aspirin, the aspirin is converted to salicylate, and salicylate becomes highly concentrated in the cortex and papillae of the kidney. Salicylate depletes stores of glutathione. With the cellular glutathione depleted, the reactive metabolite of acetaminophen then produces lipid peroxidases and arylation of tissue proteins, ultimately resulting in necrosis of the papillae. MFO, mixed function oxidases. (Redrawn from Kincaid-Smith P, Nanra RS: Lithium-induced and analgesic-induced renal diseases. In Schrier RW, Gottschalk CW [editors]: *Diseases of the kidney,* ed 5, Boston, 1993, Little Brown, pp 1099-1129; and Duggin GG: Combination analgesic-induced kidney disease: the Australian experience, *Am J Kidney Dis* 28[Suppl 1]:S39-S47, 1996.)

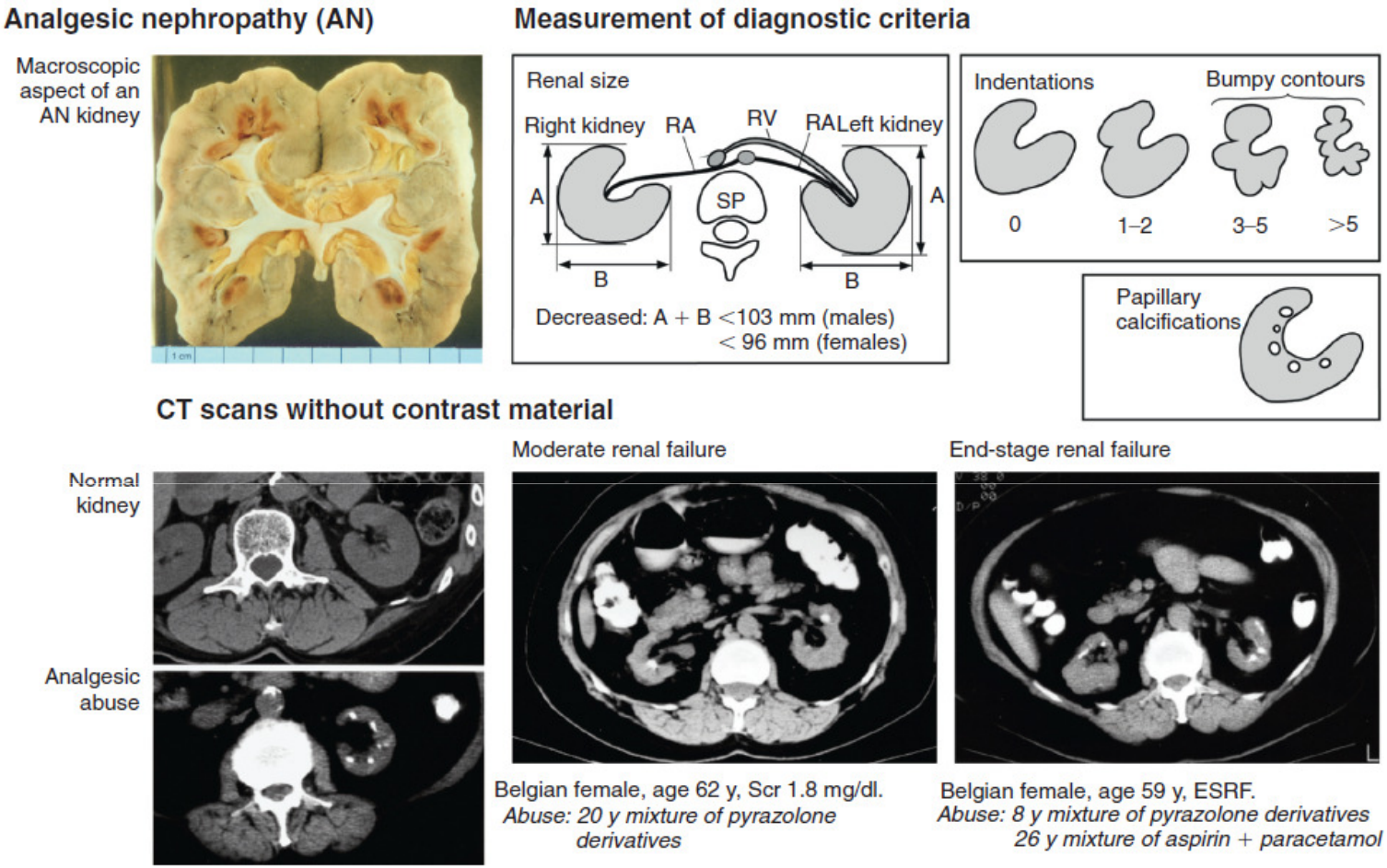

Figure 36.3 Renal imaging criteria of analgesic nephropathy (AN) as observed in a postmortem kidney and in computed tomography (CT) scans without contrast material. These criteria include a decreased renal size, bumpy contours, and papillary calcifications. RA, Renal artery; RV, renal vein; SP, spine. (Adapted from De Broe ME, Elseviers MM: Analgesic nephropathy. *N Engl J Med* 338:446-452, 1998.)

Leptospirosis 鉤端螺旋體病

- Caused by Leptospira
- Taiwan: Leptospira santarosai, most frequently encountered
- From benign infection to Weil's disease (jaundice, myocarditis, pulmonary hemorrhage), rhabdomyolysis
- Early phase: 3-7 days, fever, myalgia, 80-90% symptom free after this phase; 10% progressed to 2nd phase
- Second phase: 4-30 days, Weil's disease
- Kidney: AKI (40-60%), tubulointerstitial nephritis, ATN, 鈉鉀排出增加
- Diagnosis: serology with leptospiral Ab with MAT, PCR, culture, ELISA
- IV Penicillin(可使重症死亡率降低), oral Doxycycline

Renal cell carcinoma

- 60-80 y/o
- Factors: tobacco, exposure to cadmium, asbestos, petroleum, obesity, acquired cystic kidney disease, analgesic abuse nephropathy
- Classified
  - by types: clear (von Hippel-Lindau loss of function), granular, spindle, oncocytic
  - by growth pattern: acinar, papillary, sarcomatoid

Table 41.1 Pathologic Classification of Renal Cell Carcinoma

Carcinoma Type	Growth Pattern (Incidence, %)	Cell of Origin	Cytogenetic Characteristics	
			Major	Minor
Clear cell	Acinar or sarcomatoid (75-85)	Proximal tubule	–3p	+5, +7, +12, –6p, –8p –9, –14q, –Y
Chromophilic*	Papillary or sarcomatoid (12-14)	Proximal tubule	+7, +17, –Y	+12, +16, +20, –14
Chromophobic	Solid, tubular, or sarcomatoid (4-6)	Intercalated cell of cortical collecting duct	Hypodiploidy	—
Oncocytic	Typified by tumor nests (2-4)	Intercalated cell of cortical collecting duct	Undetermined†	—
Collecting duct	Papillary or sarcomatoid (1)	Medullary collecting duct	Undetermined†	—

Renal cell carcinoma

- 25% have metastasis at the time of presentation
- Paraneoplastic syndromes: fever, secondary amyloidosis, anemia, hepatic dysfunction in **absence** of metastatic disease (Stauffer's syndrome: ALK-P, alfa globulin, AST/ALT, aPTT上升), erythrocytosis, hypercalcemia
- 最常轉移的地方是lung, 接著為lymph node, bone, liver

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2020
Kidney Cancer

NCCN Guidelines Index
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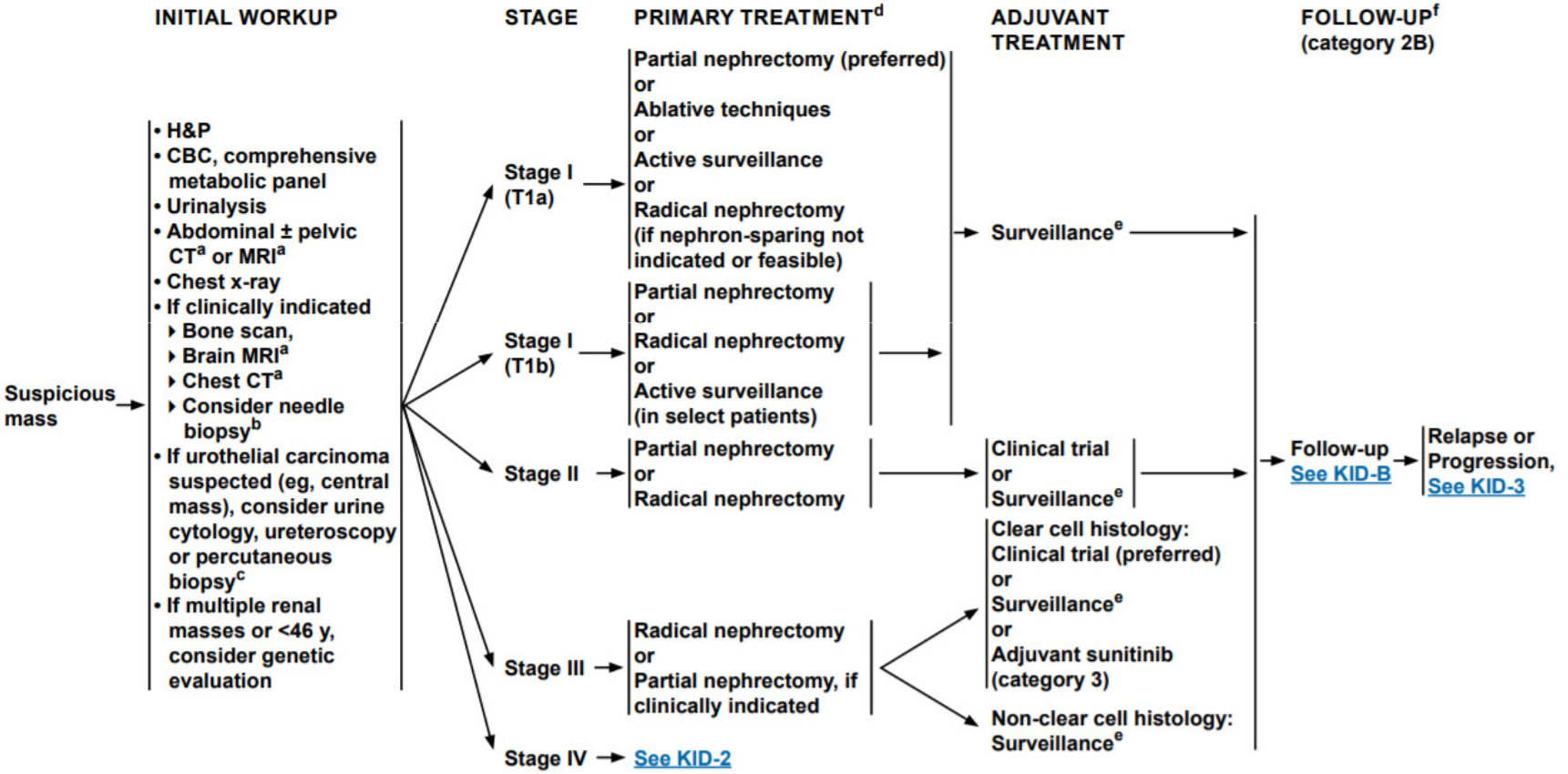
Discussion



Bone marrow transplanted nephropathy

- **Radiation** nephropathy after BMT: 10-Gy, single-fraction dose is sufficient to cause
- Acute radiation nephropathy (most frequent): 6-12 months, HUS-like picture, severe hypertension, edema, microangiopathic hemolytic anemia, thrombocytopenia, decreased renal function, proteinuria, microscopic hematuria
- Chronic radiation nephropathy: 18 months to years, hypertension, mild hemolytic anemia, loss of renal function

BK virus

- Human polyomavirus
- Common opportunistic infection in solid/HCT patients
- 50% BK viruria in patients undergoing HCT
- Hemorrhagic cystitis, tubular atrophy/fibrosis, lymphocytic infiltrate with intranuclear BK virus inclusion body
- Diagnosis: blood/urine viral titers
- Treatment: minimization of immunosuppression

Low protein diet

- Reduce hyperfiltration: **constriction** of afferent arteriole, decrease glomerular plasma flow and proteinuria
- Prevent glomerular hypertrophy
- Attenuate progression of diabetic nephropathy
- Antifibrotic effect

Low protein diet

- Change intestinal flora
- Improve insulin resistance
- Cause minimal evidence of malnutrition in MDRD study
- Did **not** complicate task of consuming sufficient calories (30-35kcal/kg/day)

Table 61.2 Dietary Requirements for Patients with Chronic Kidney Disease

Patients	Protein Requirement	Comments
Normal adults or those with uncomplicated CKD	RDA, 0.8 g protein/kg/day	30-35 kcal/kg/day needed to use dietary protein efficiently
Symptomatic CKD patients, those with complications	Minimum, 0.6 g protein/kg/day or 0.3 g/kg/day + ketoacids or a mixture of essential amino acids	Adjustments for specific problems (e.g., diabetes, hyperphosphatemia)
CKD patients with loss of muscle mass	0.8 g protein/kg/day	
CKD patients with proteinuria	<0.8 g protein/kg/day + 1 g protein/g proteinuria	This is the maximum needed. Even less dietary protein may be sufficient.

CKD, Chronic kidney disease; RDA, recommended daily allowance.

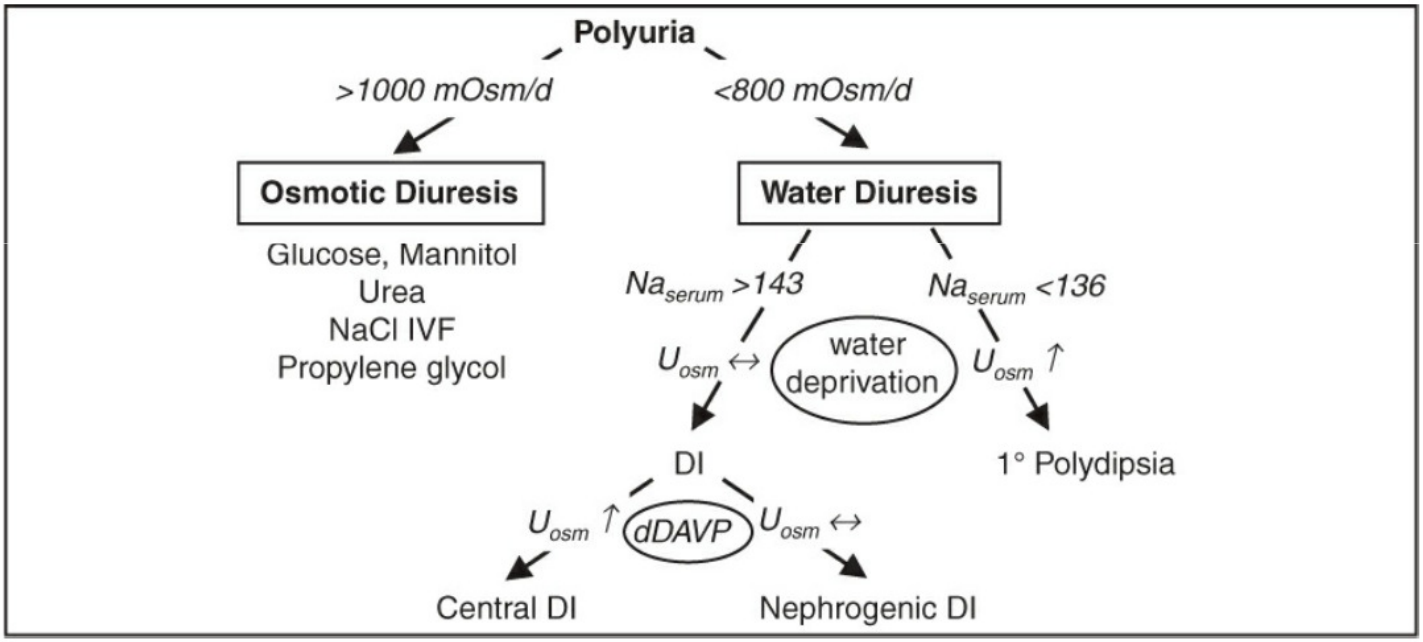
BENEFICIAL RESPONSES TO REDUCED DIETARY PROTEIN IN CHRONIC KIDNEY DISEASE OR AFTER KIDNEY TRANSPLANTATION

To determine if the decreased loss of kidney function found in animals fed LPDs also occurs in humans, clinical trials have examined the benefits of reducing dietary protein on nutritional status and the progressive loss of kidney function in patients with CKD. Unfortunately, some of the published studies are of low methodologic quality because they were retrospective studies with only a small number of patients or serious design flaws. Based on standards of adequate quality, we examined more than 80 trials from which 10 RCTs[326-335] and five meta-analyses[336-340] were identified. With these data, we addressed the question of whether dietary protein restriction slows the progression of CKD.[339] In discussing these reports, we will use the more general term *slowed progression of kidney disease* rather than *slowed the loss of kidney function*. The GFR (the gold standard of kidney function) was determined in just a few studies. Instead, outcomes in reported trials were based on estimating differences in changes in serum creatinine levels or the degree of proteinuria.

Aging & bladder change

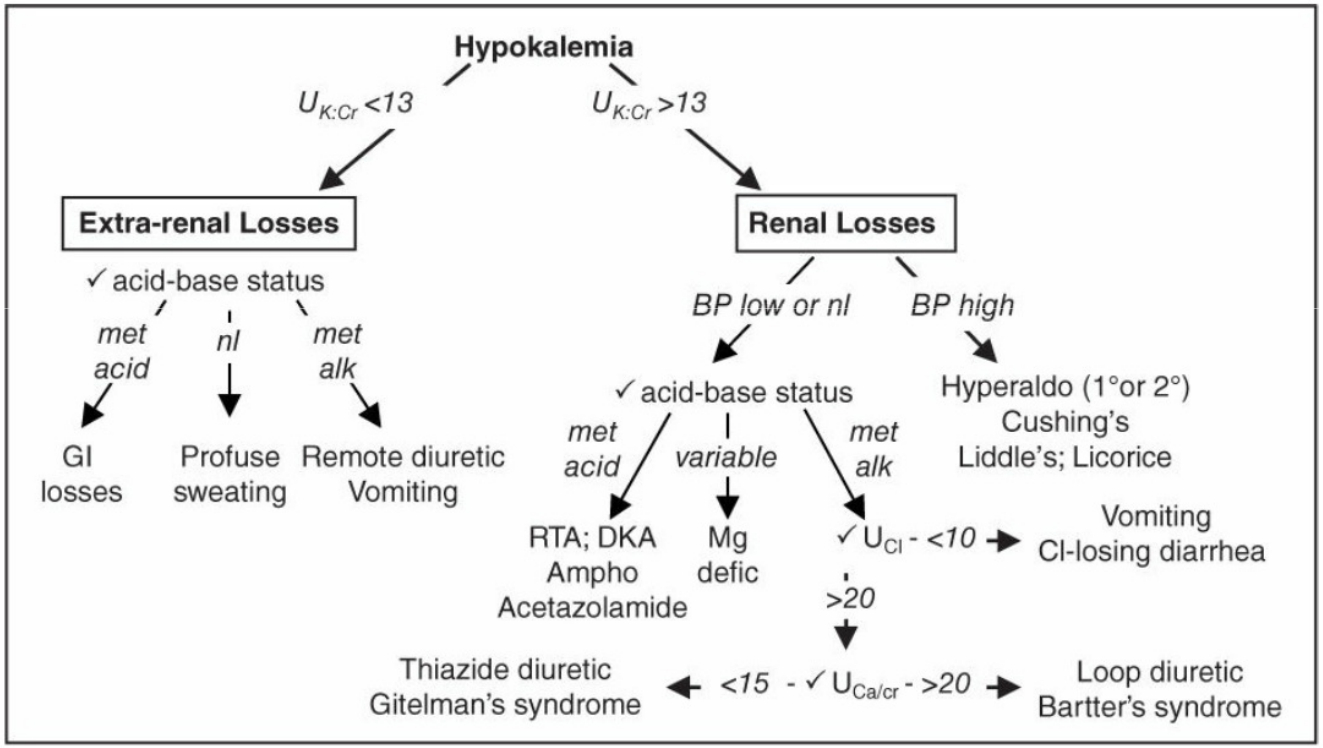
- The bladder wall changes
  - Elastic tissue becomes tough and the bladder becomes less stretchy
  - Bladder **cannot** hold as much urine as before
- The bladder muscles weaken
- The urethra can become blocked
  - In women: weakened muscles that cause the bladder or vagina to fall out of position (prolapse)
  - In men: enlarged prostate gland

Thank You !


Polyuria
>1000 mOsm/d
<800 mOsm/d
Osmotic Diuresis
Water Diuresis
Glucose, Mannitol
Urea
NaCl IVF
Propylene glycol
Na_{serum} >143
Na_{serum} <136
U_{osm} ↔
water deprivation
U_{osm} ↑
DI
1° Polydipsia
U_{osm} ↑
dDAVP
U_{osm} ↔
Central DI
Nephrogenic DI

Hyperkalemia

Increased potassium release from cells
Pseudohyperkalemia
Metabolic acidosis
Insulin deficiency, hyperglycemia, and hyperosmolality
Increased tissue catabolism
Beta blockers
Exercise
Hyperkalemic periodic paralysis
Other
Overdose of digitalis or related digitalis glycosides
Red cell transfusion
Succinylcholine
Arginine hydrochloride
Activators of ATP-dependent potassium channels (eg, calcineurin inhibitors, diazoxide, minoxidil, and some volatile anesthetics)
Reduced urinary potassium excretion
Reduced aldosterone secretion
Reduced response to aldosterone
Reduced distal sodium and water delivery
Effective arterial blood volume depletion
Acute and chronic kidney disease
Other
Selective impairment in potassium secretion
Gordon's syndrome
Ureterojejunostomy


Hypokalemia
$U_{K:Cr}$ <13
$U_{K:Cr}$ >13
Extra-renal Losses
Renal Losses
✓ acid-base status
met acid
nl
met alk
GI losses
Profuse sweating
Remote diuretic
Vomiting
BP low or nl
BP high
✓ acid-base status
Hyperaldo (1°or 2°)
Cushing's
Liddle's; Licorice
met acid
variable
met alk
RTA; DKA
Ampho
Acetazolamide
Mg defic
✓ U_{Cl} - <10
Vomiting
Cl-losing diarrhea
>20
Thiazide diuretic
Gitelman's syndrome
<15 - ✓ $U_{Ca/cr}$ - >20
Loop diuretic
Bartter's syndrome

HyperCa

Parathyroid mediated
Primary hyperparathyroidism (sporadic)
Inherited variants
Multiple endocrine neoplasia (MEN) syndromes
Familial isolated hyperparathyroidism
Hyperparathyroidism-jaw tumor syndrome
Familial hypocalciuric hypercalcemia
Tertiary hyperparathyroidism (renal failure)
Non-parathyroid mediated
Hypercalcemia of malignancy
PTHrP
Increased calcitriol (activation of extrarenal 1-alpha-hydroxylase)
Osteolytic bone metastases and local cytokines
Vitamin D intoxication
Chronic granulomatous disorders
Increased calcitriol (activation of extrarenal 1-alpha-hydroxylase)
Medications
Thiazide diuretics
Lithium
Teriparatide
Abaloparatide
Excessive vitamin A
Theophylline toxicity
Miscellaneous
Hyperthyroidism
Acromegaly
Pheochromocytoma
Adrenal insufficiency
Immobilization
Parenteral nutrition
Milk-alkali syndrome

Hypocalcemia

- Low PTH (hypoparathyroidism): genetic, postsurgical, autoimmune, infiltration, radiation-induced, hungry bone syndrome, HIV infection
- High PTH (secondary hyperparathyroidism to hypocalcemia): vit D deficiency/resistance, PTH resistance (pseudohypoparathyroidism), renal disease, loss Ca from circulation (tumor lysis, pancreatitis, osteoblastic metastasis)
- Drugs: Cinacalcet, EDTA, Foscarnet, Fluoride poisoning
- Mg disorder

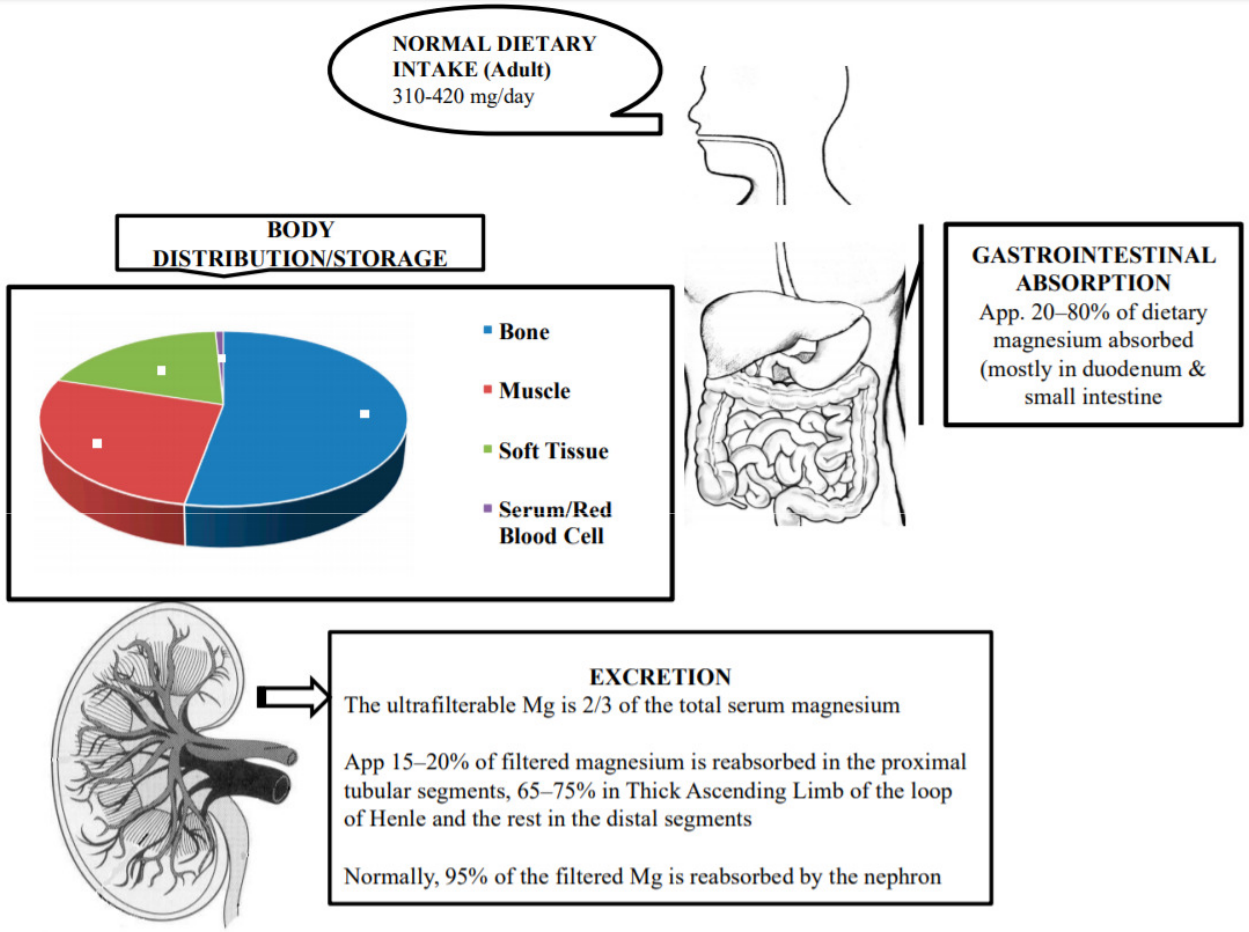


Figure 1. Physiology of magnesium.

Hypermagnesemia

- Kidney impairment
- Mg infusion, oral ingestion
- Enemas
- Miscellaneous: primary hyperparathyroidism, FHH, diabetic ketoacidosis, hypercatabolic states, Lithium ingestion, milk-alkali syndrome, adrenal insufficiency, HELIX syndrome

Table 1. Causes of hypomagnesemia.

Decreased Intake
Decreased Dietary consumption
Alcohol Dependence
Parenteral Nutrition
Redistribution from Extracellular to Intracellular Compartment:
Refeeding Syndrome
Hungry Bone Syndrome
Treatment of Diabetic Ketoacidosis
Acute Pancreatitis
Gastrointestinal Losses:
Diarrhea
Vomiting
Nasogastric suction
Fistulas
Malabsorption
Small bowel bypass surgery
Proton Pump Inhibitors
Renal Losses:
Familial:
Bartter syndrome, Gitelman syndrome, Familial hypomagnesemia with hypercalciuria and nephrocalcinosis (FHHNC)
Acquired:
Medications: Thiazide Diuretic, Aminoglycoside Antibiotics, Amphotericin B, Cisplatin, Pentamidine, Tacrolimus, Cyclosporine
Alcohol Dependence, Hypercalcemia

Table 3. Clinical manifestations of hypomagnesemia.

Neuromuscular/Nervous System:
Positive Chvostek's And Trousseau's Signs, Tremor, Fasciculations, Tetany, Headaches, Seizures, Fatigue, Generalized Fatigue, Asthenia
Cardiovascular:
Atherosclerotic Vascular Disease/Coronary Artery Disease
Arrhythmias: Torsades de pointes, PR prolongation, progressive QRS widening and diminution of T-waves
Hypertension
Congestive Heart Failure
Endocrine: ***Altered Glucose Homeostasis/Diabetic Complications***
Osteoporosis
Biochemical/Others:
Hypokalemia
Hypocalcemia
Asthma
Nephrolithiasis

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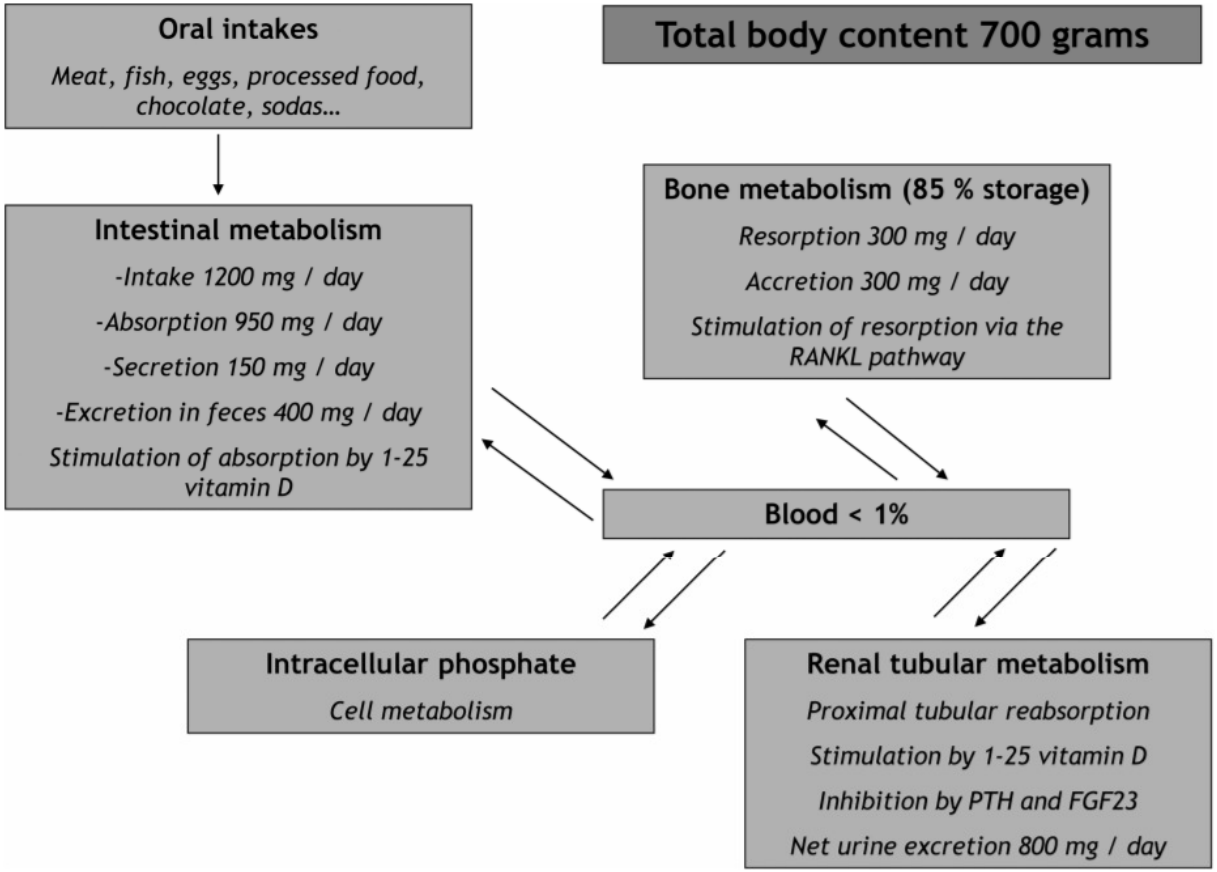

Figure 1.
Overview of phosphate physiology in adults
PTH: parathyroid hormone
FGF23: Fibroblast Growth Factor 23
RANKL: Receptor Activator for Nuclear Factor κ B Ligand

Box 1

Causes of Hyperphosphatemia

Pseudohyperphosphatemia

- Hyperglobulinemia
- Hyperlipidemia
- Hyperbilirubinemia

Acute phosphate load

- Exogenous
  - ◊ Phosphate-containing laxatives
  - ◊ Vitamin D toxicity
- Endogenous
  - ◊ Tumor lysis syndrome
  - ◊ Rhabdomyolysis
  - ◊ Hemolysis
  - ◊ Lactic acidosis
  - ◊ Diabetic ketoacidosis

Decreased filtered load of phosphate

- Kidney failure

Abnormal tubular phosphate handling

- Hypoparathyroidism
- Pseudohypoparathyroidism
- Familial tumoral calcinosis

Etiologies of hypophosphatemia

	Acute hypophosphatemia	Chronic hypophosphatemia
Decreased phosphate intake		Inadequate parenteral nutrition Nutritional defects
Decreased intestinal absorption		Vitamin D deficiency Vitamin D-dependent rickets Chronic anti-acid therapy Intestinal malabsorption Chronic liver disease Alcoholism
Increased renal wasting of primary renal disease	After renal transplantation (first weeks) Acute volume expansion	De De Toni Debre Fanconi syndrome Dent disease Toxic (ifosfamide, platin salts, diuretics, glucocorticoids, retroviral therapies in HIV patients, acetazolamide)
Hyperparathyroidism		Primary and secondary hyperparathyroidisms
Increased FGF23 serum levels		Hypophosphatemic rickets Tumor-induced osteomalacia Fibrous dysplasia Mac Cune Albright syndrome Toxic (saccharated ferric oxide)
Redistribution of phosphate between the different compartments	After bone marrow transplantation Acute leukemia and lymphoma Correction of diabetic ketoacidosis Refeeding Acute respiratory alkalosis Hungry bone syndrome	Treatment with erythropoiesis-stimulating agents in patients with cirrhosis
Miscellaneous	Severe sepsis Extensive burns Inadequate dialysis Acute paracetamol overdose Salicylate poisoning Hypothermia	