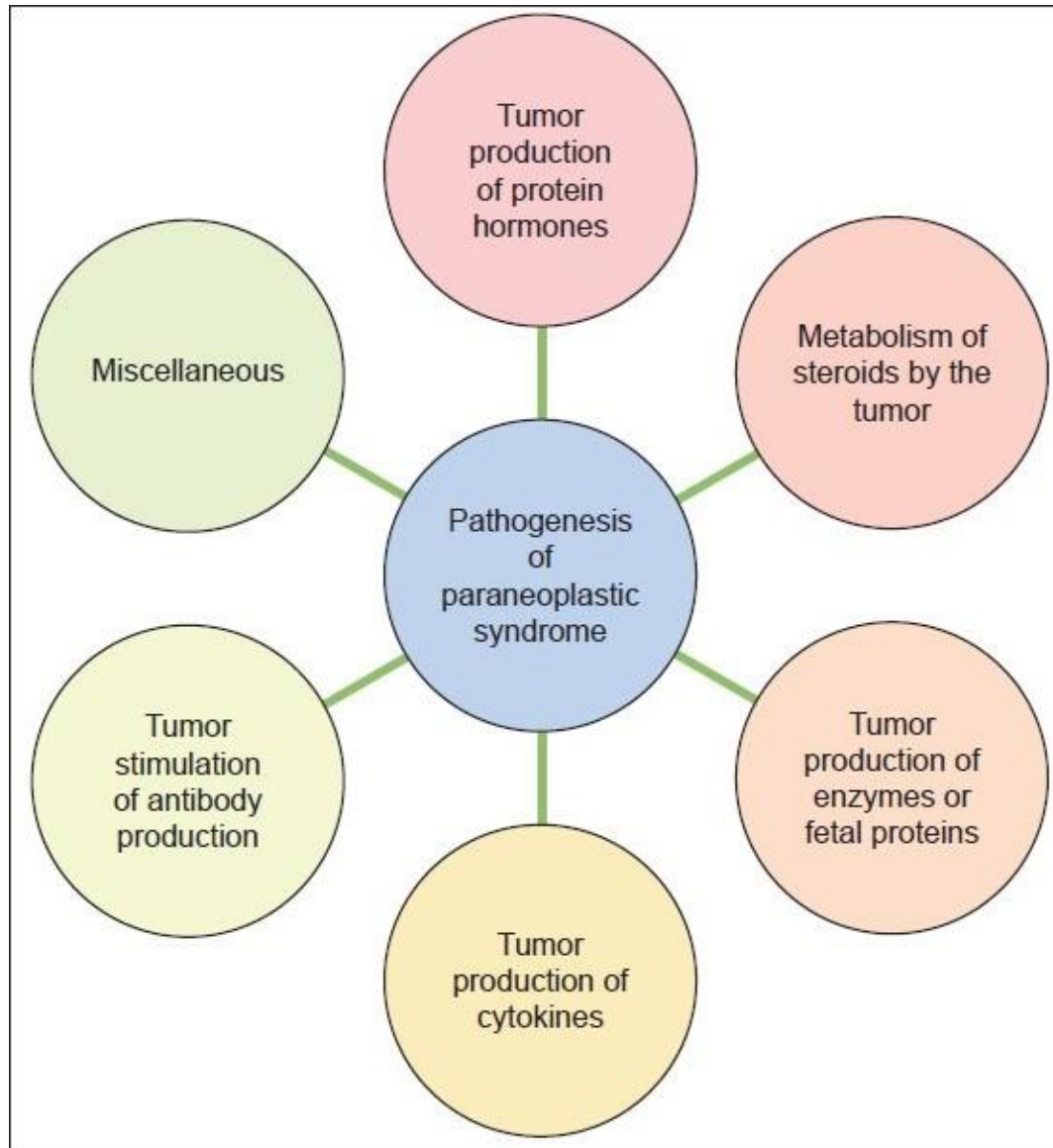
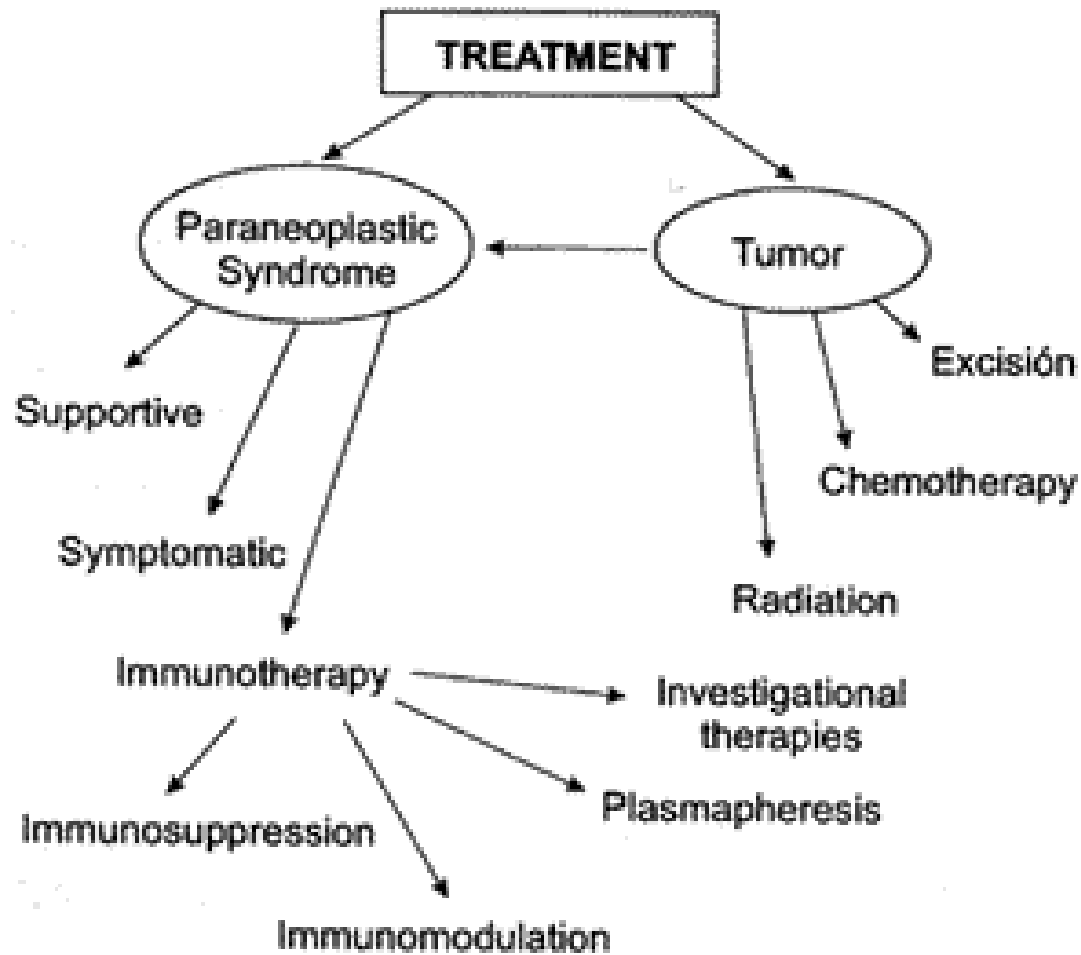
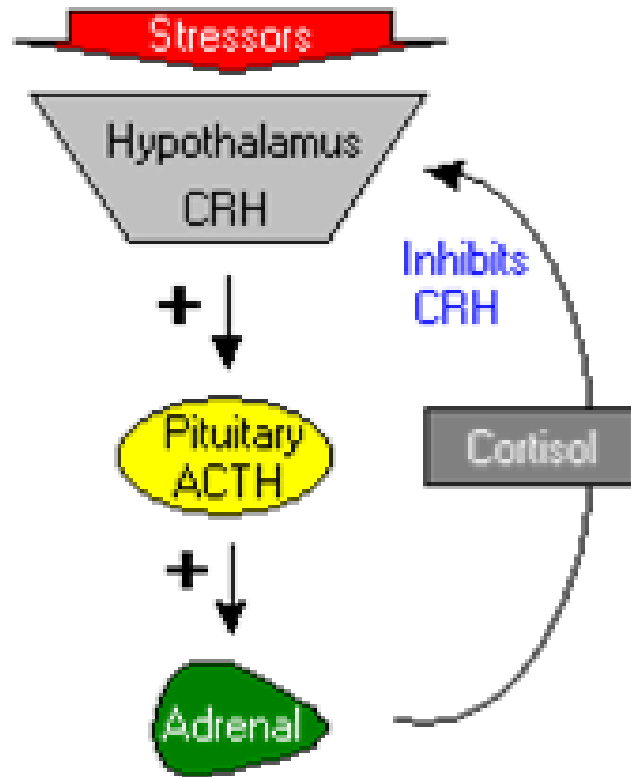


Ενδοκρινικές εκδηλώσεις των κακοηθειών

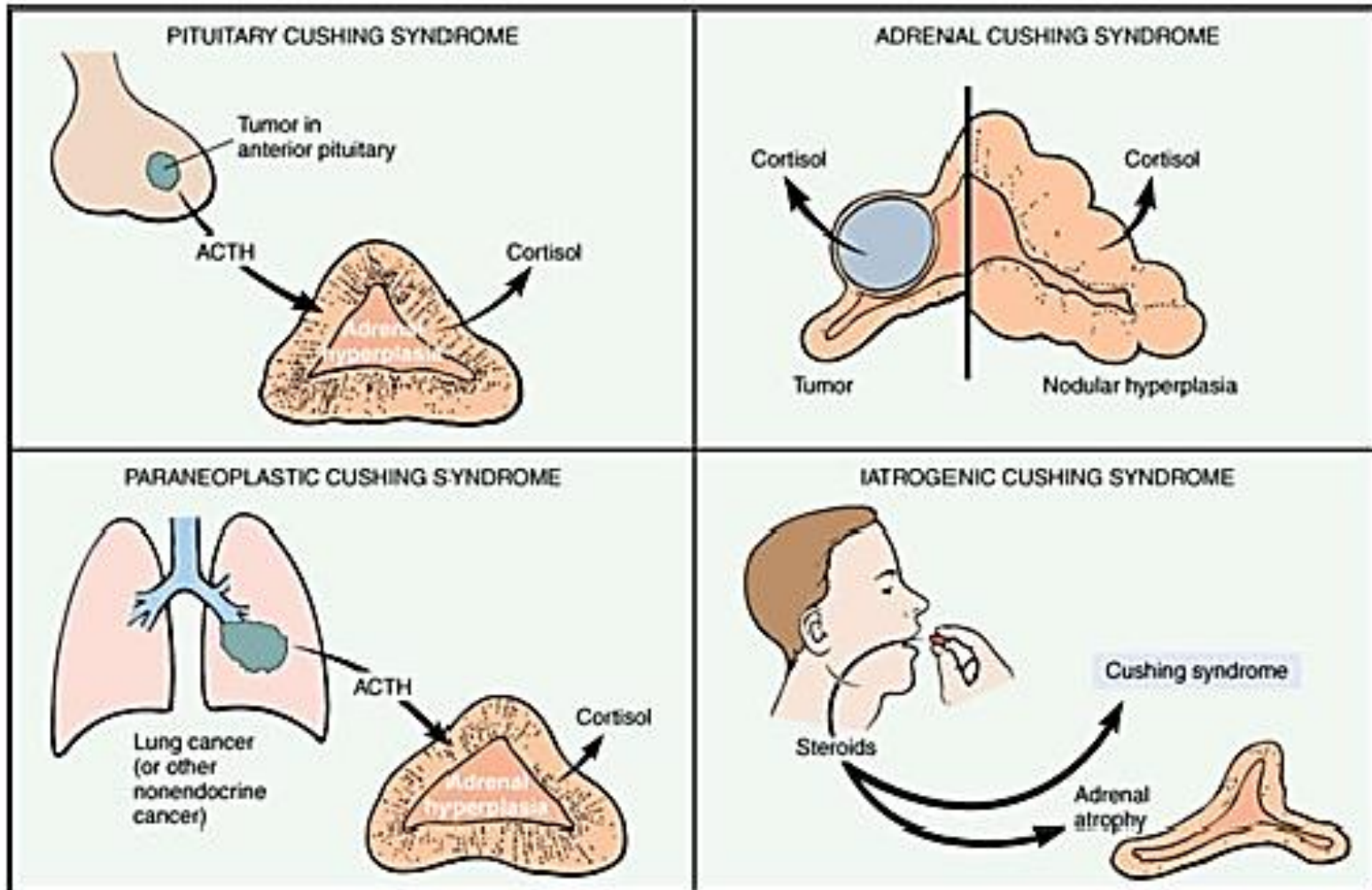
Γιώργος Παπαξοΐνης
Παθολόγος Ογκολόγος
Β' Πανεπιστημιακή Παθολογική Κλινική
ΓΝΑ «Ιπποκράτειο»

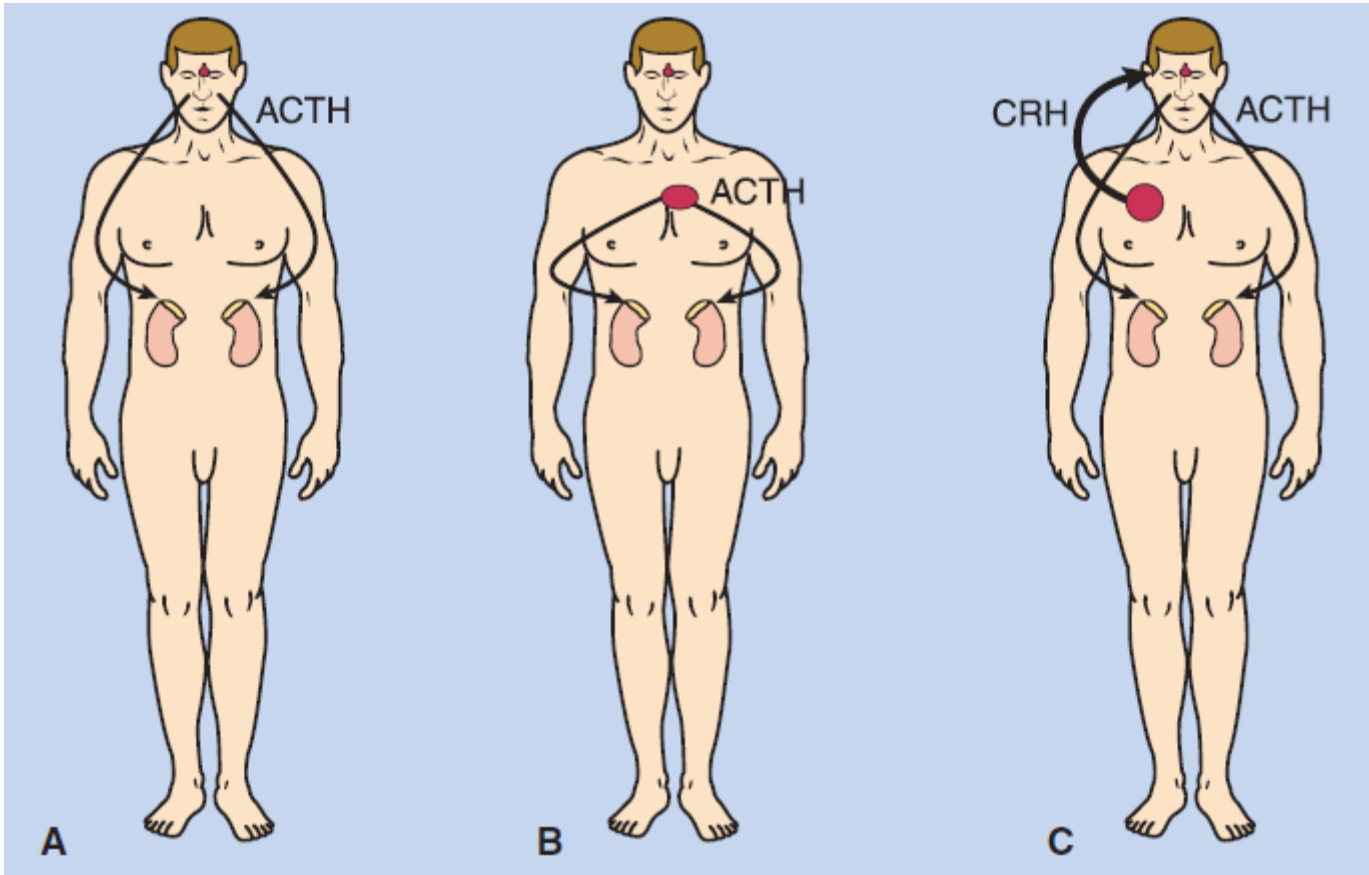






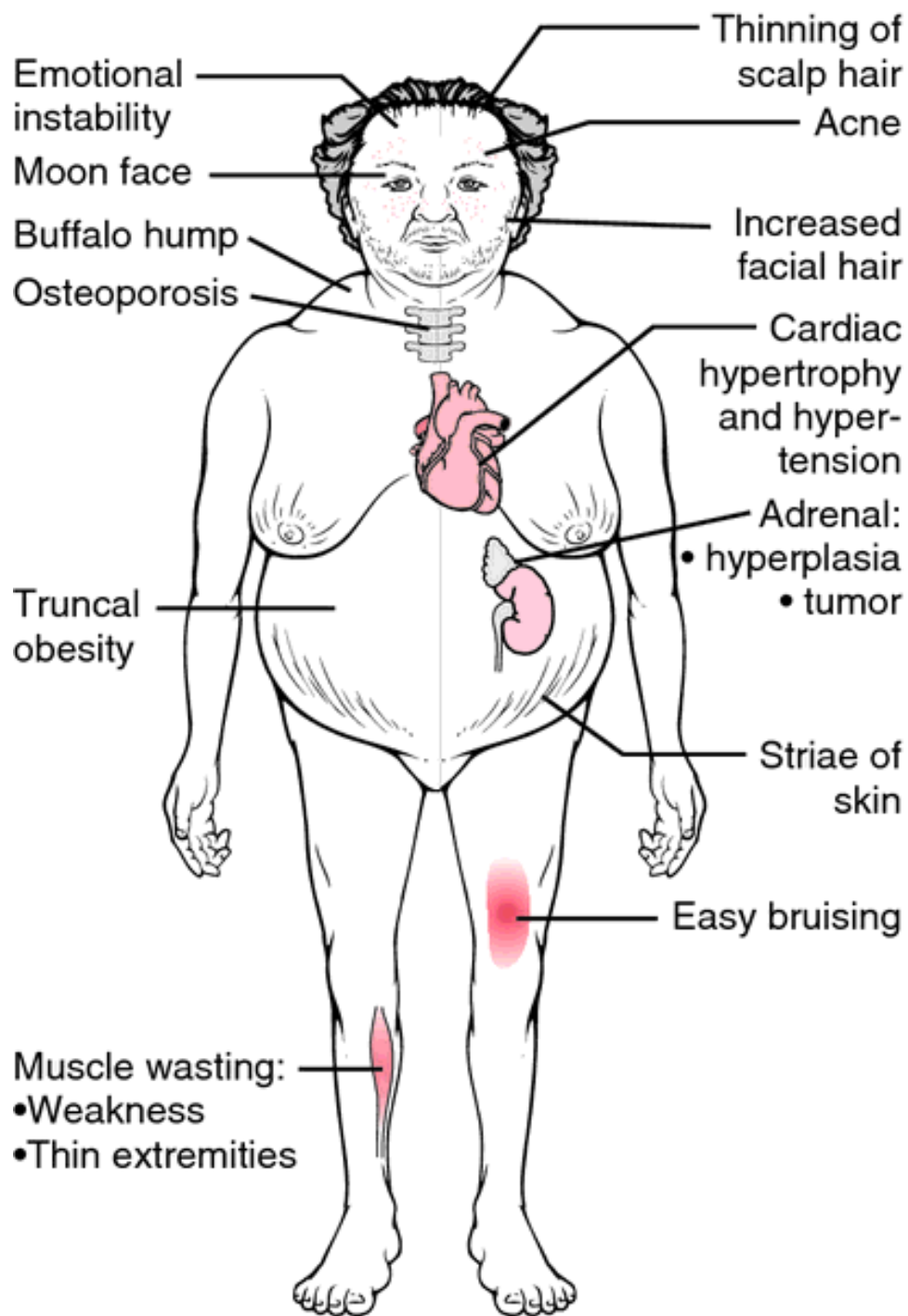
Αίτια συνδρόμου Cushing





Παρανεοπλασματικό Cushing

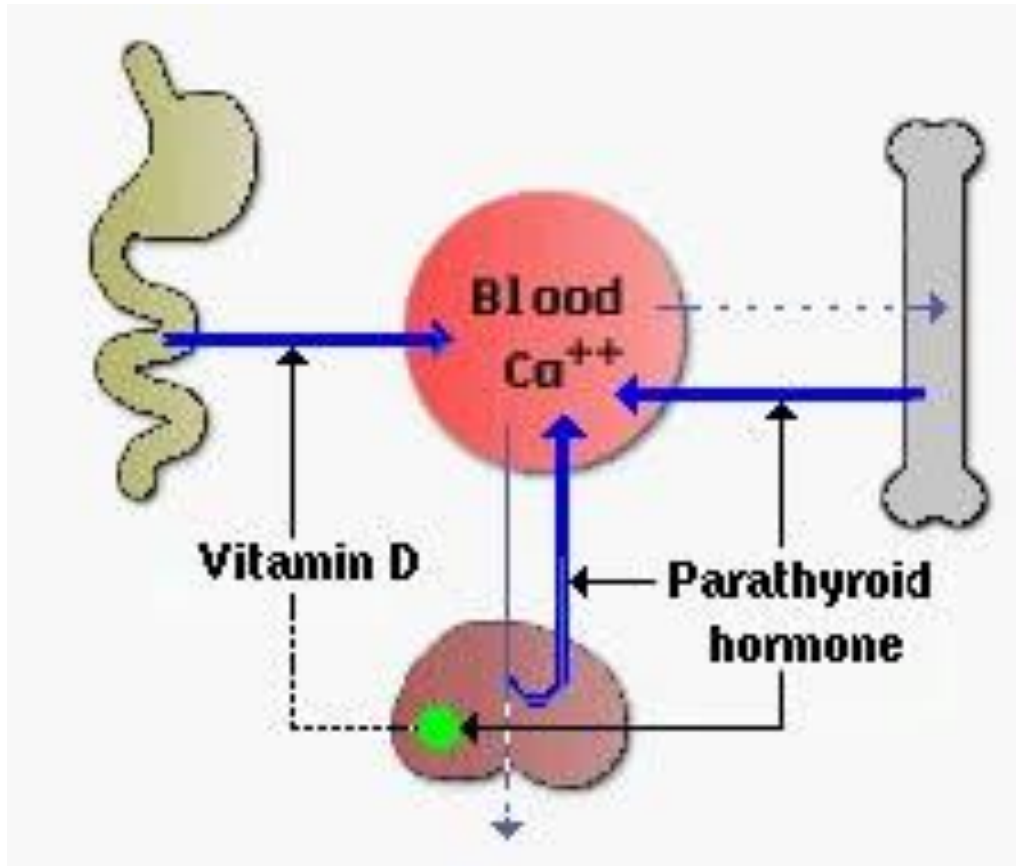
- Έκτοπη έκκριση ACTH (SCLC, πνευμονικό καρκινοειδές, μυελοειδής καρκίνος θυρεοειδούς, νησιδίωμα, φαιοχρωμοκύττωμα, γαγγλιονεύρωμα)
- Έκτοπη έκκριση CRH (μυελοειδής καρκίνος θυρεοειδούς, παραγαγγλίωμα, κα προστάτη, νησιδίωμα)



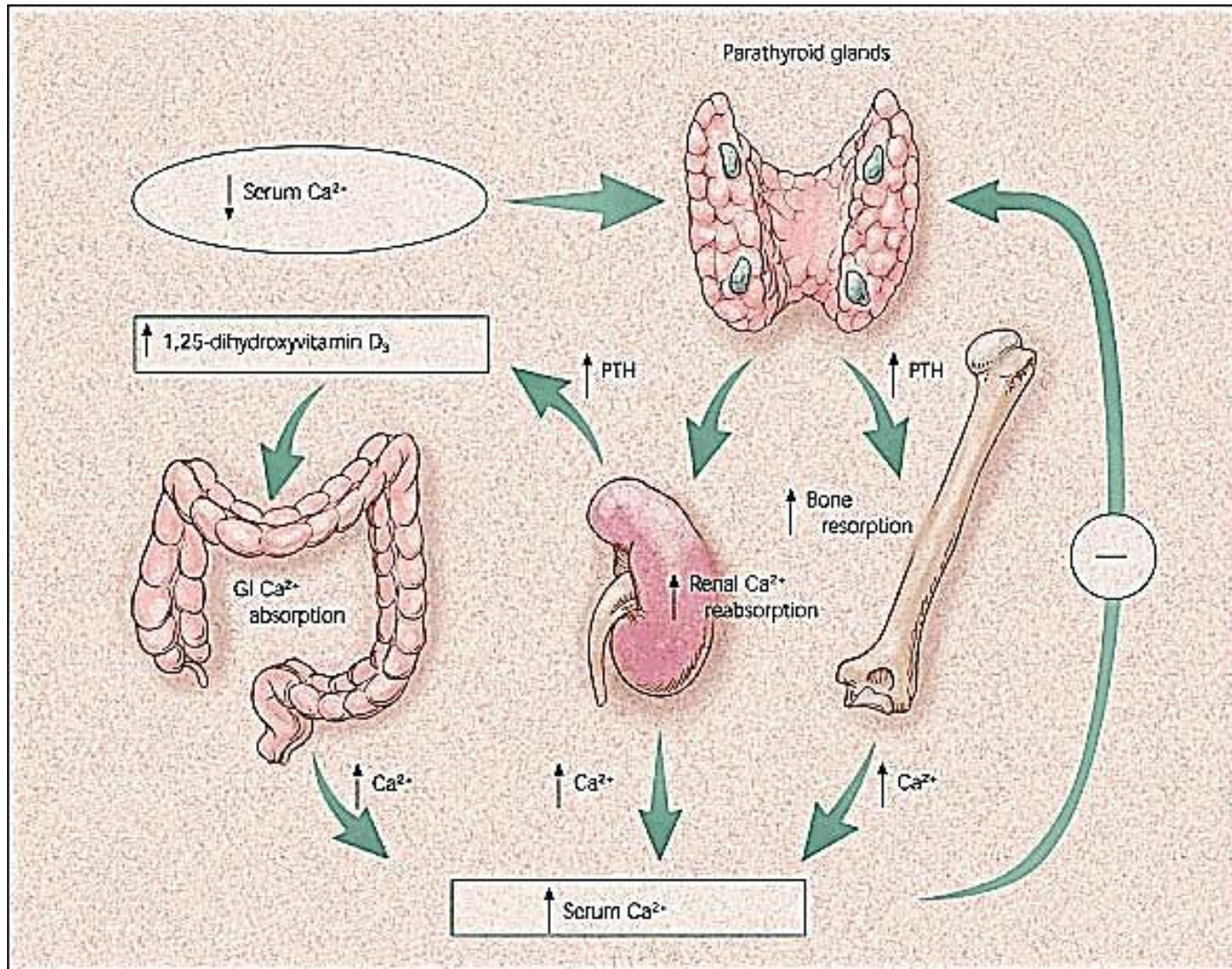
Παρανεοπλασματικό Cushing

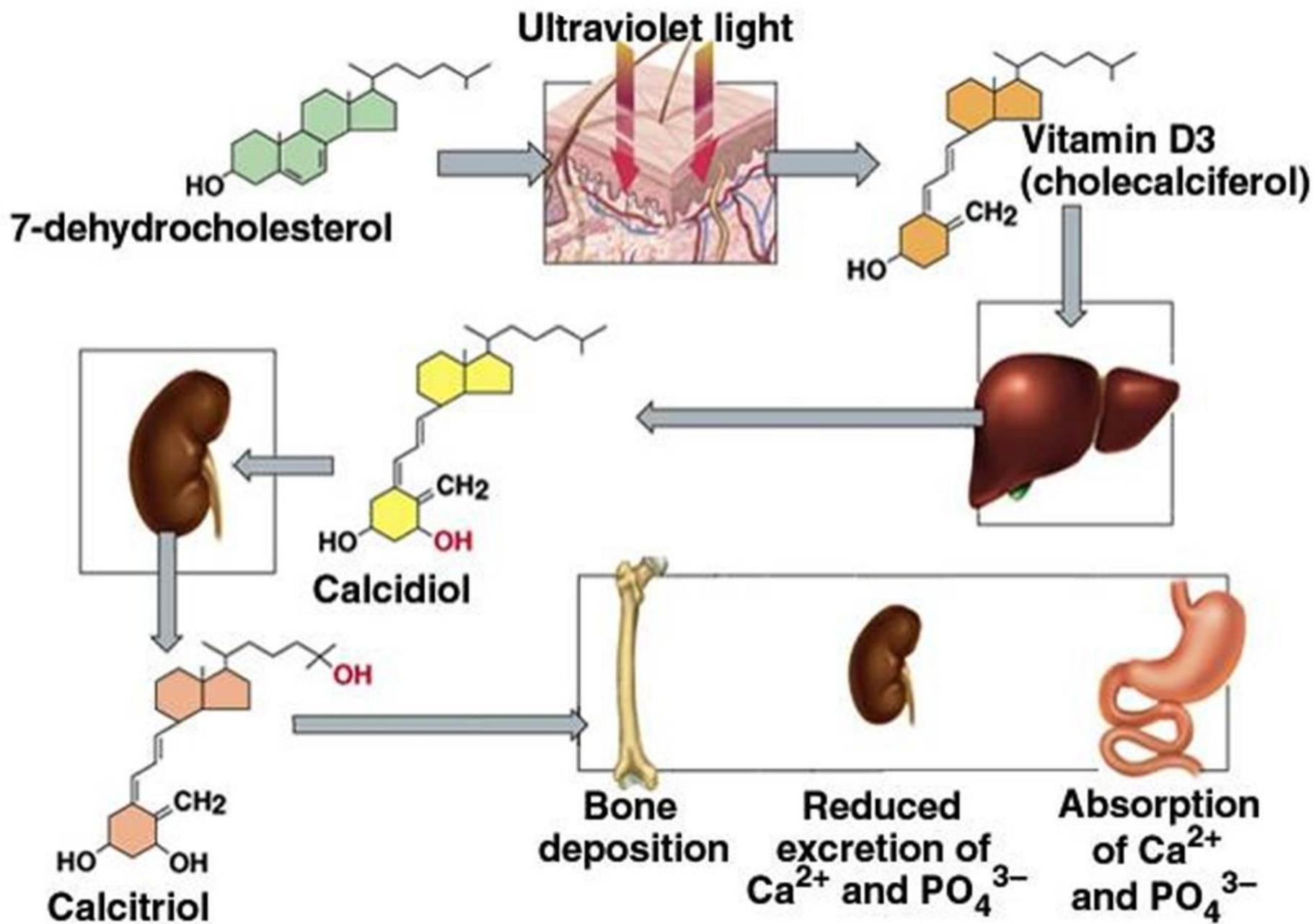
- Διάγνωση:
 - δοκιμασία πρόκλησης με δεξαμεθαζόνη
- Θεραπεία:
 - Αντινεοπλασματική θεραπεία
 - Μετυραπόνη, αμινογλουτεθιμίδη, κετοκοναζόλη
 - Λαπαροσκοπική επινεφριδιεκτομή

Υπερασβεστιαμία



Μεταβολισμός ασβεστίου

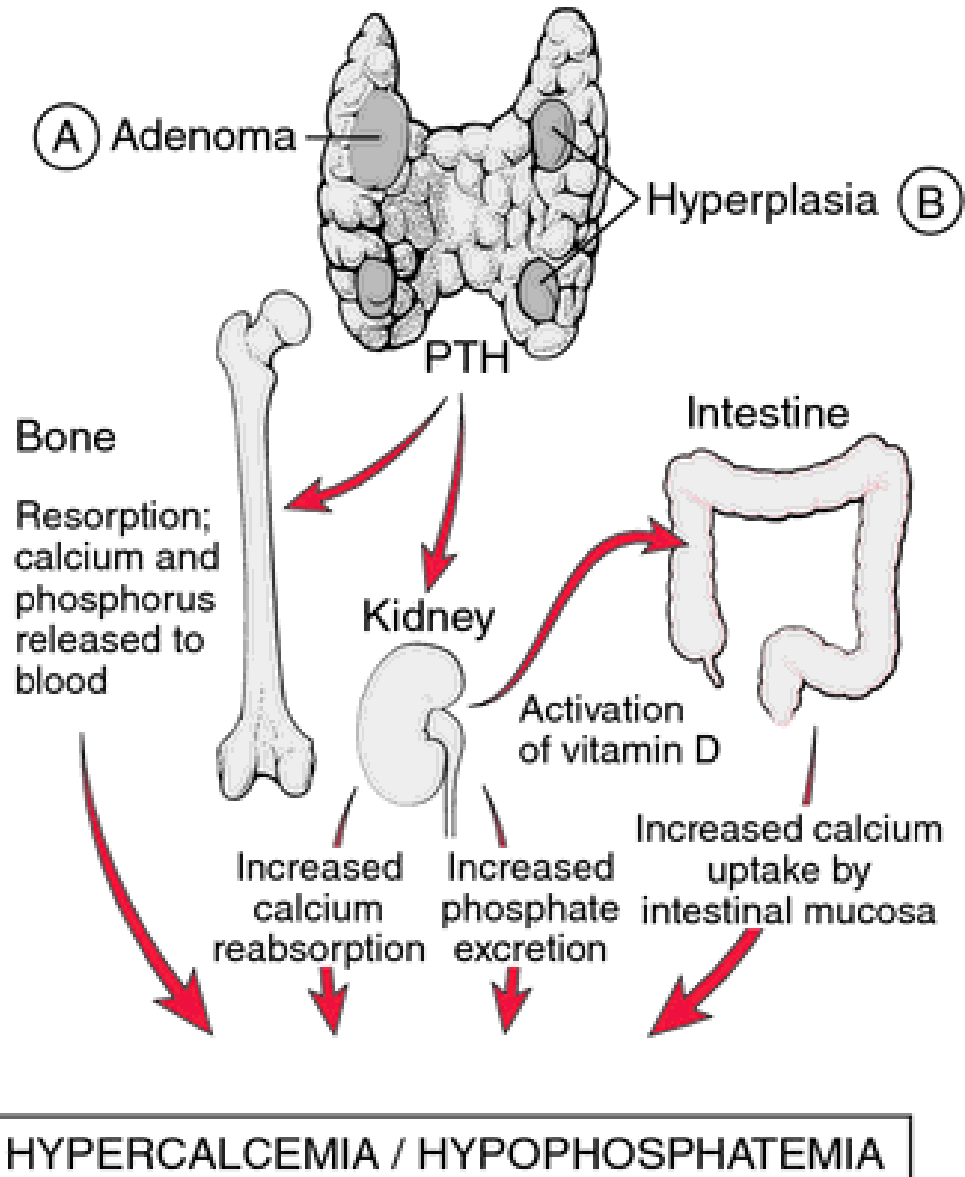


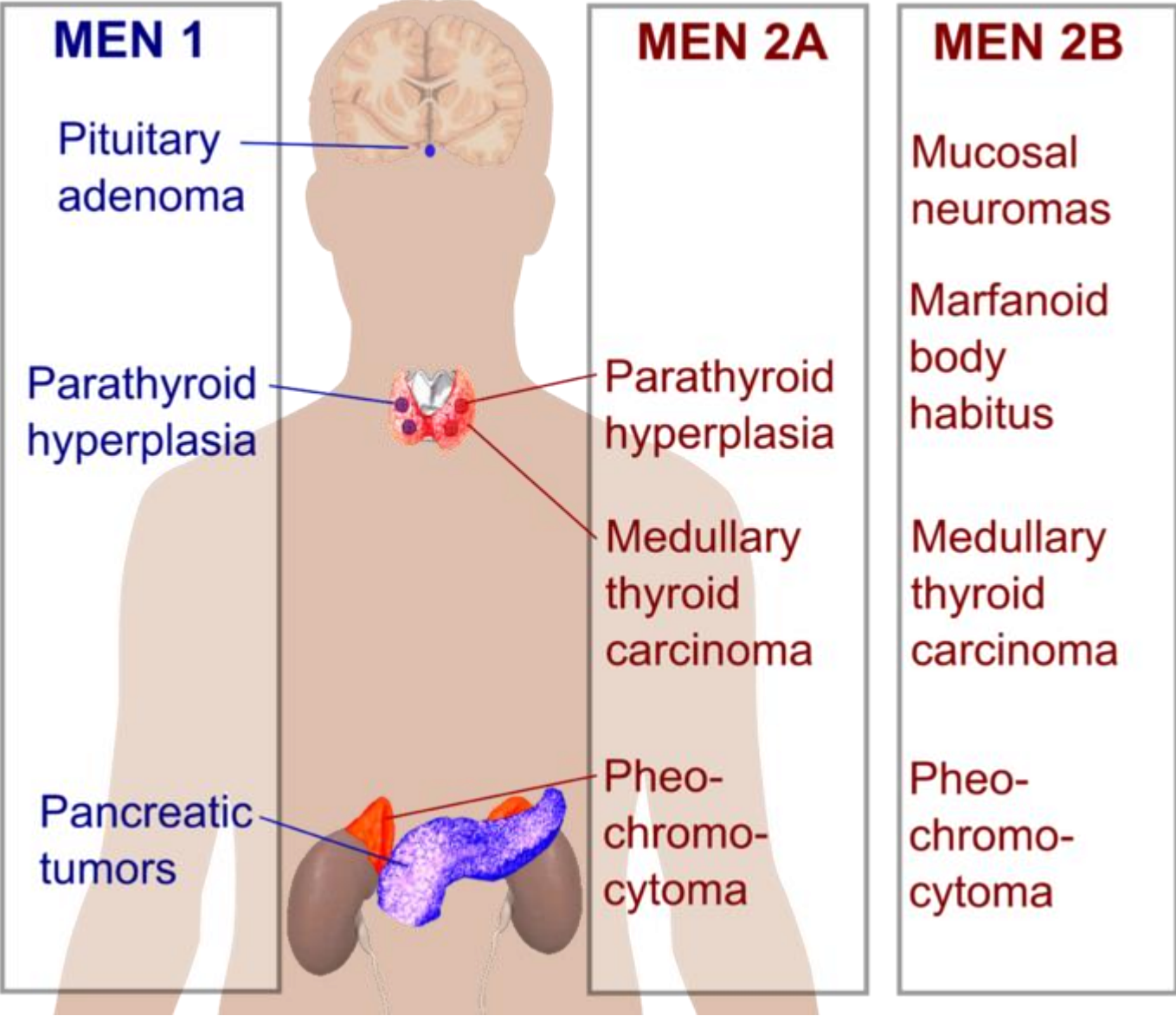


Αίτια υπερασβεστιαμίας

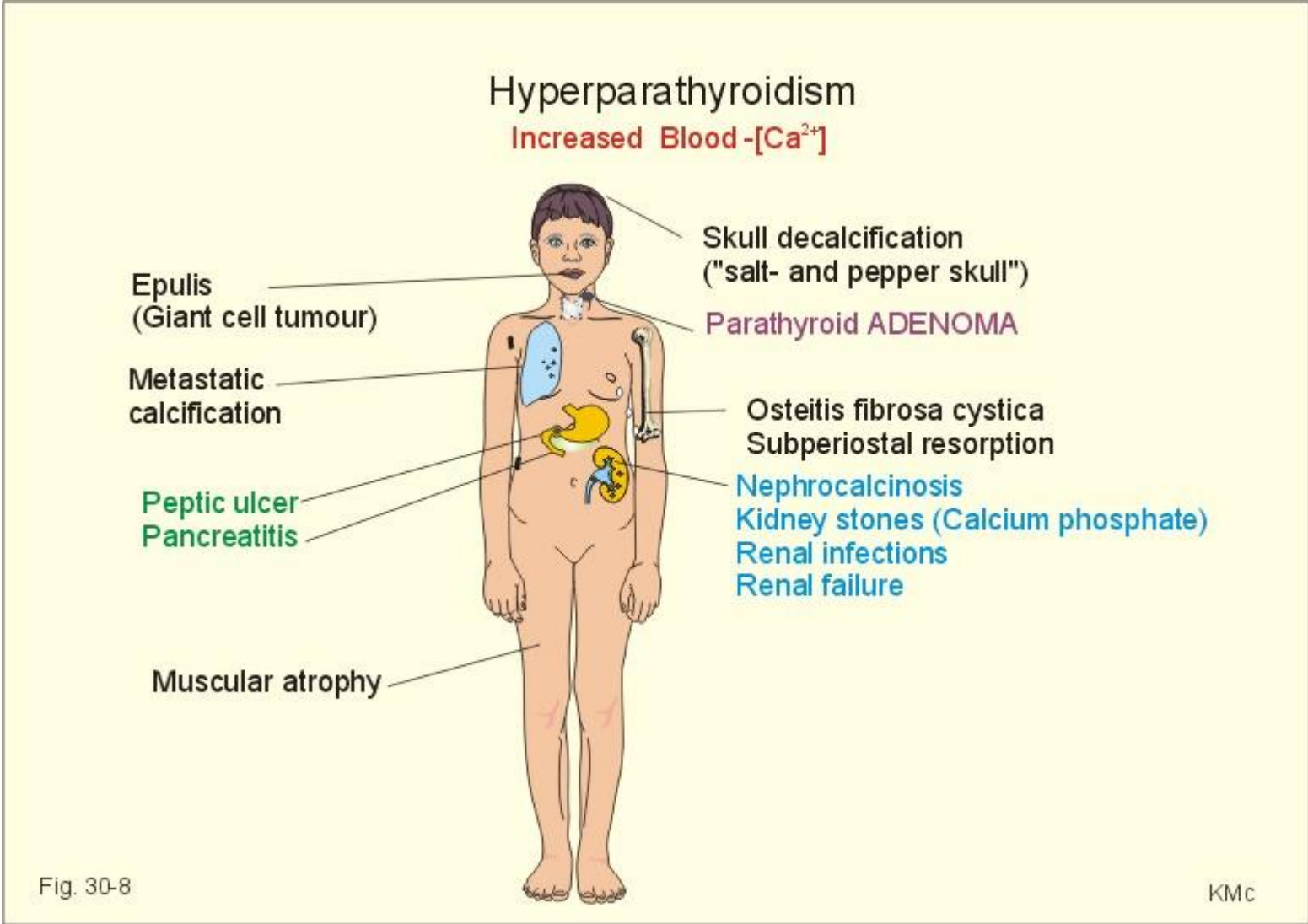
- Πρωτοπαθής υπερπαραθυρεοειδισμός
- Έκτοπη παραγωγή PTHrP (πλακώδη κα, όγκοι μαστού, νεφρών, προστάτη, μελάνωμα, νευροενδοκρινείς)
- Έκτοπη έκκριση καλσιτριόλης (λέμφωμα)
- Οστεολυτικές εντοπίσεις (κα μαστού, π.μυέλωμα)

Πρωτοπαθής υπερπαραθυρεοειδισμός

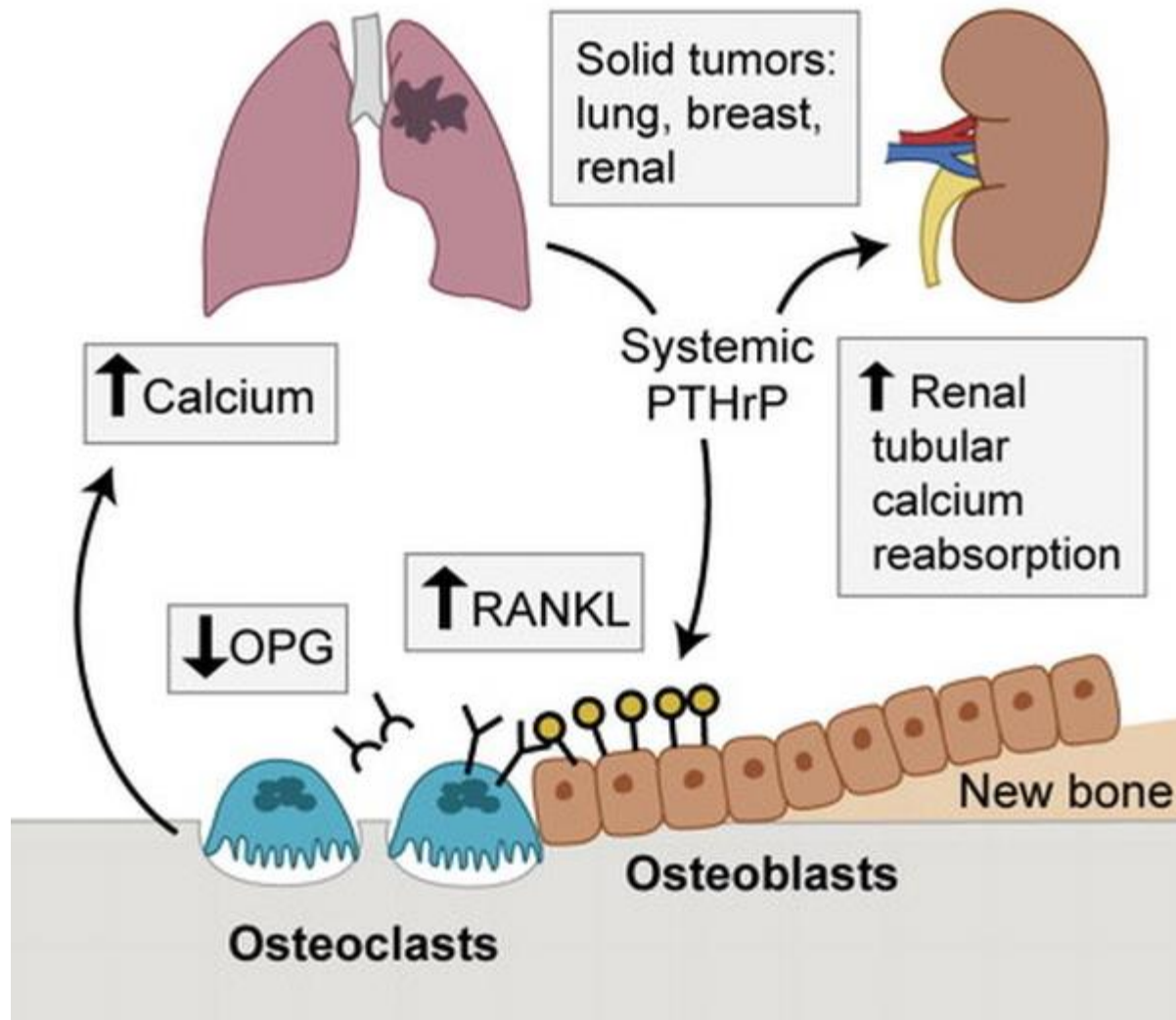




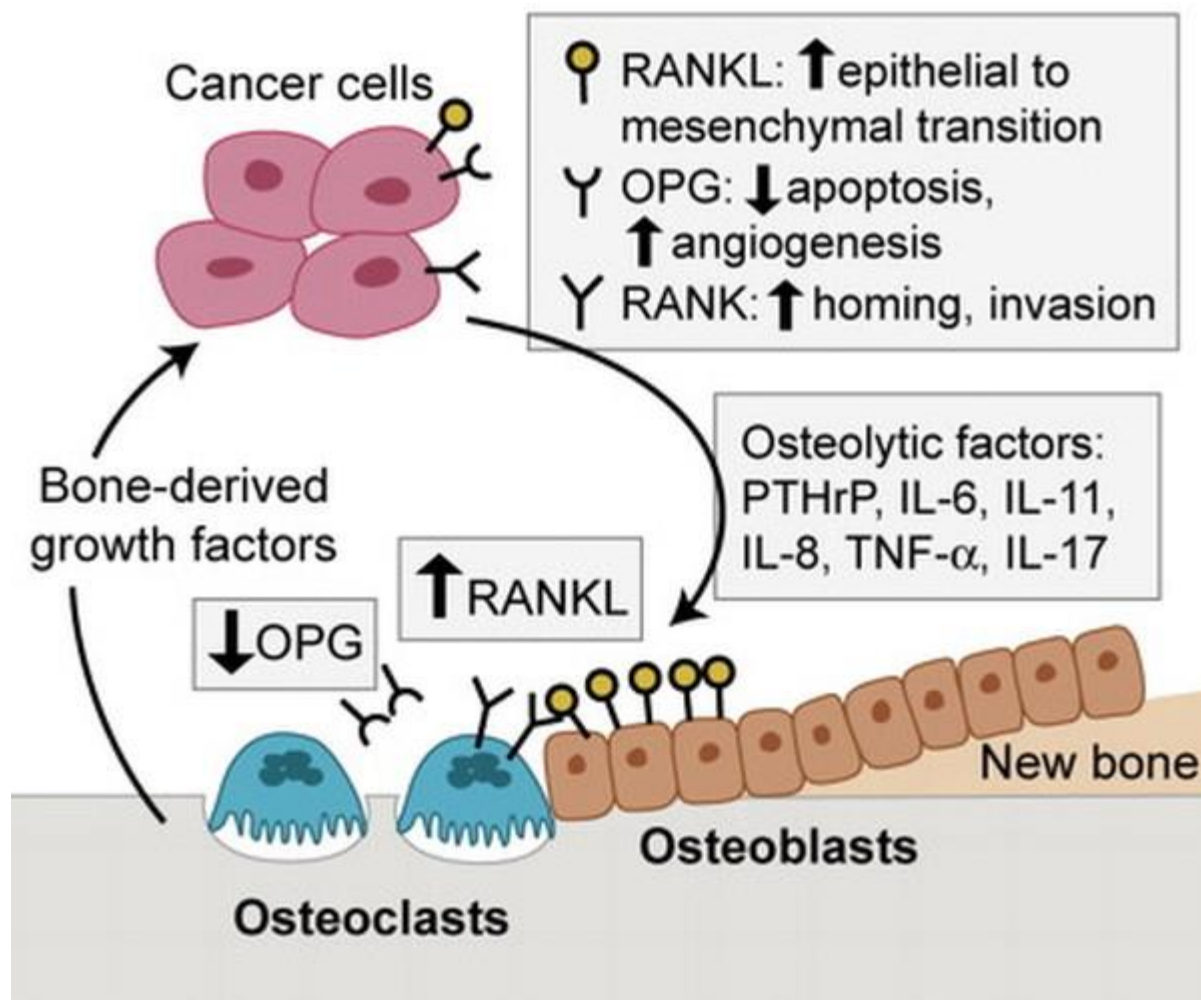
Κλινικές εκδηλώσεις υπερπαραθυρεοειδισμού



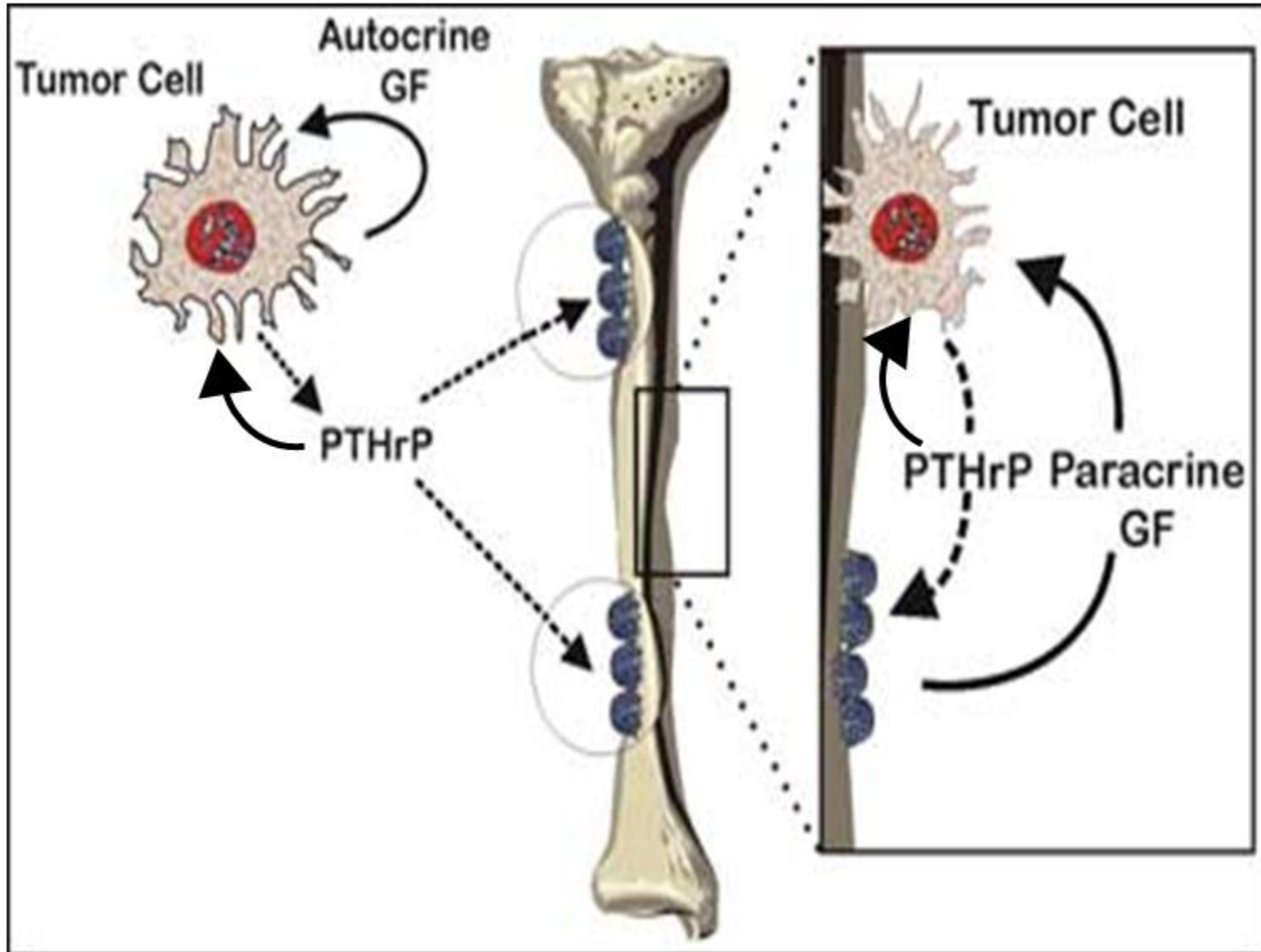
Hypercalcemia of Malignancy



Solid Tumor Bone Metastases and Myeloma



Οστεολυτικές εντοπίσεις

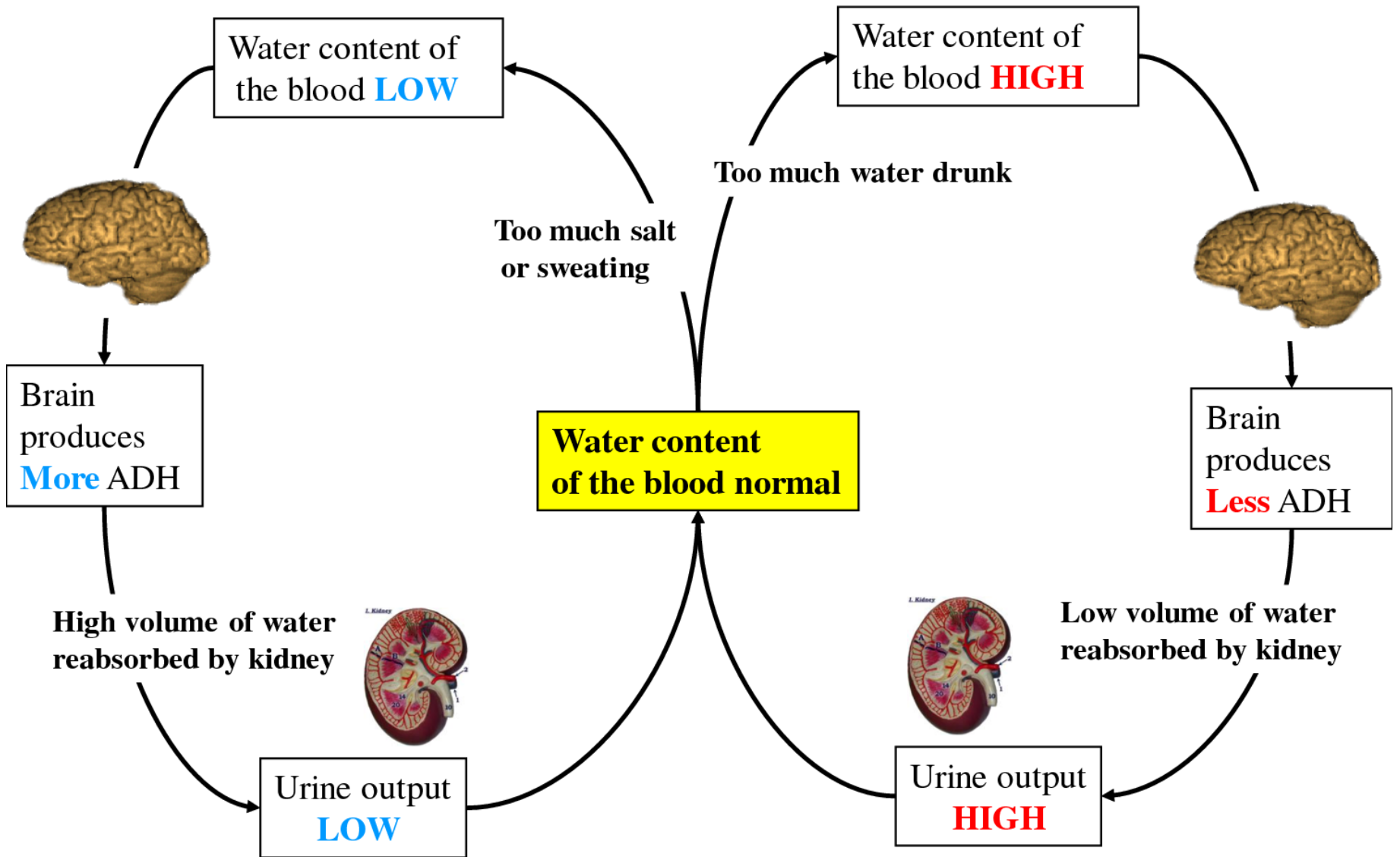


Κλινικές εκδηλώσεις υπερασβεστιαμίας

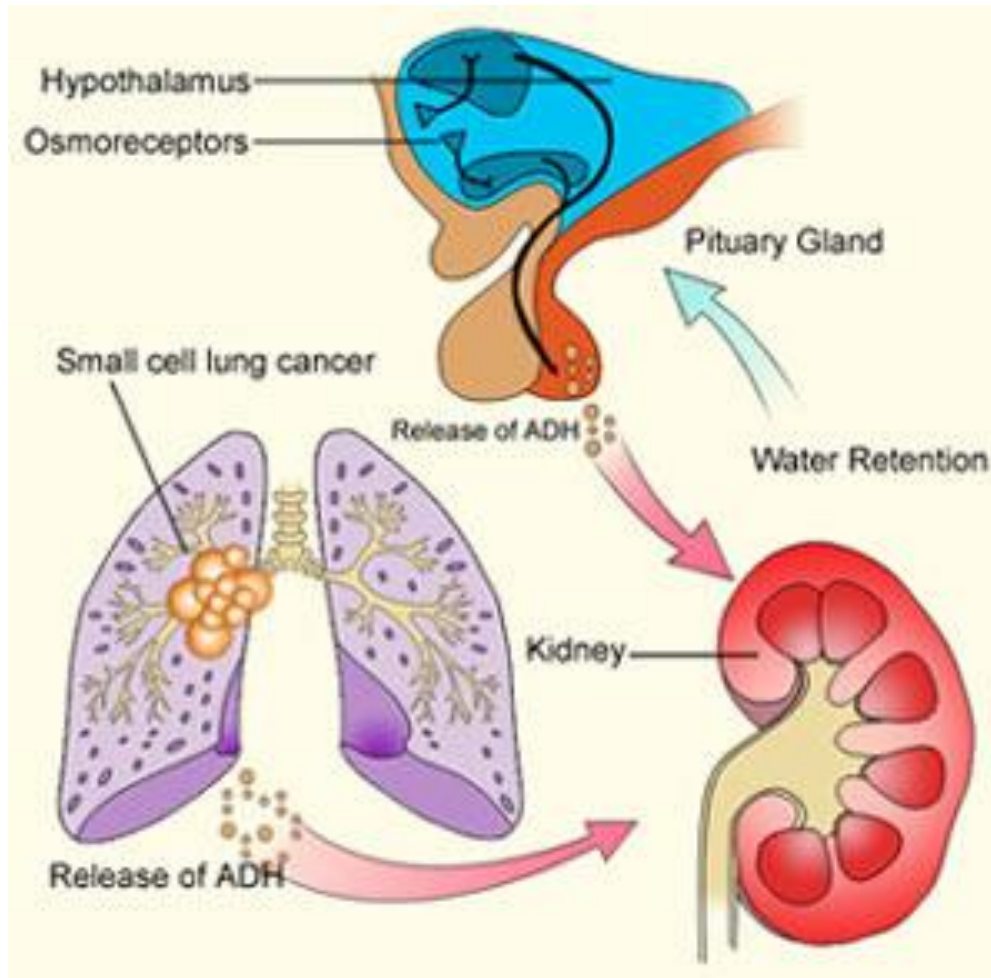
General	CNS	Cardiac	GI	Renal
Dehydration	Weakness	Bradycardia	Nausea and vomiting	Polyuria
Anorexia	Hypotonia	Short QT interval	Constipation	Nephrocalcinosis
Pruritus	Proximal myopathy	Prolonged PR interval	Ileus	–
Weight loss	Mental status changes	Wide T wave	Pancreatitis	–
Fatigue	Seizure Coma	Atrial or ventricular arrhythmia	Dyspepsia	–

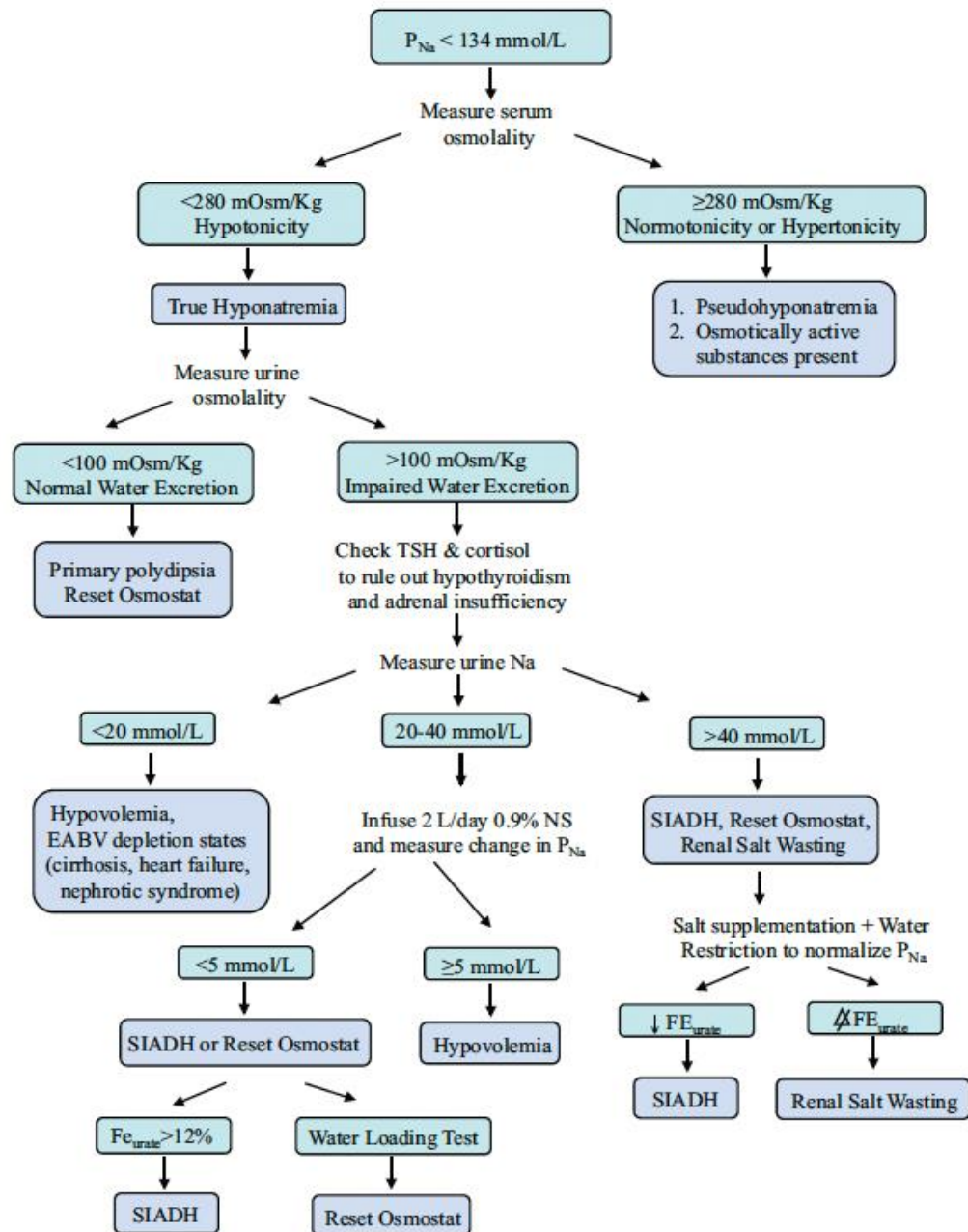
Αντιμετώπιση υπερασβεστιαμίας

- Ενυδάτωση
- Διούρηση (φουροσεμίδη)
- Καλσιτονίνη
- Ζολενδρονικό οξύ (διφωσφονικό)
- Πρεδνιζόνη (π.μυέλωμα)



Απρόσφορη έκκριση ADH





P_{Na} =plasma sodium; TSH=thyroid stimulating hormone; FE_{urate} =fractional excretion of urate; EABV=effective arterial blood volume; NS=normal saline; SIADH=syndrome of inappropriate antidiuretic hormone.

Hypervolemic	Euvolemic	Hypovolemic
<ul style="list-style-type: none"> •CHF •Cirrhosis •Renal failure •Nephrotic syndrome 	<ul style="list-style-type: none"> •Glucocorticoid deficiency •Hypothyroidism •SIADH •Tumors •CNS disorders •Drug-induced* •Pulmonary diseases (infections; ventilatory or mechanical impairments) •AIDS •Prolonged strenuous exercise •Senile atrophy •Idiopathic •Beer potomania •Very low protein intake •Excessive water intake •Primary polydipsia •Freshwater drowning 	<ul style="list-style-type: none"> •Renal sodium losses •Diuretics •Cerebral salt-wasting •Salt-wasting nephropathy •Bicarbonaturia •Glucosuria •Ketonuria •Mineralocorticoid deficiency† •Extrarenal sodium losses •Gastrointestinal losses (vomiting, diarrhea) •Sweat losses (endurance exercise) •Third space losses (pancreatitis, burns, bowel obstruction)
<p>*Common: nicotine, tricyclics, DDAVP, oxytocin, angiotensin-converting enzyme inhibitors, carbamazepine, cyclophosphamide, vincristine, Ecstasy, omeprazole, serotonin reuptake inhibitors.</p> <p>†Mineralocorticoid deficiency of many causes including autoimmune causes, adrenal hemorrhage, tuberculosis, fungal infection, cytomegalovirus infection, adrenal enzyme deficiencies.</p> <p>CHF=congestive heart failure; AIDS=acquired immune deficiency syndrome; DDAVP=desmopressin acetate; SIADH=syndrome of inappropriate antidiuretic hormone secretion.</p>		

Source: Modified from Verbalis et al.

Required criteria

- Both hypothyroidism and glucocorticoid deficiency must be ruled out
- Plasma osmolality <270 mOsm/kg water
- Inappropriate urinary concentration ($U_{osm} > 100$ mosmol/kg water)
- Euvolemic volume status
- Elevated urinary sodium (>40 mmol/l) with normal salt and water intake

Supplemental criteria

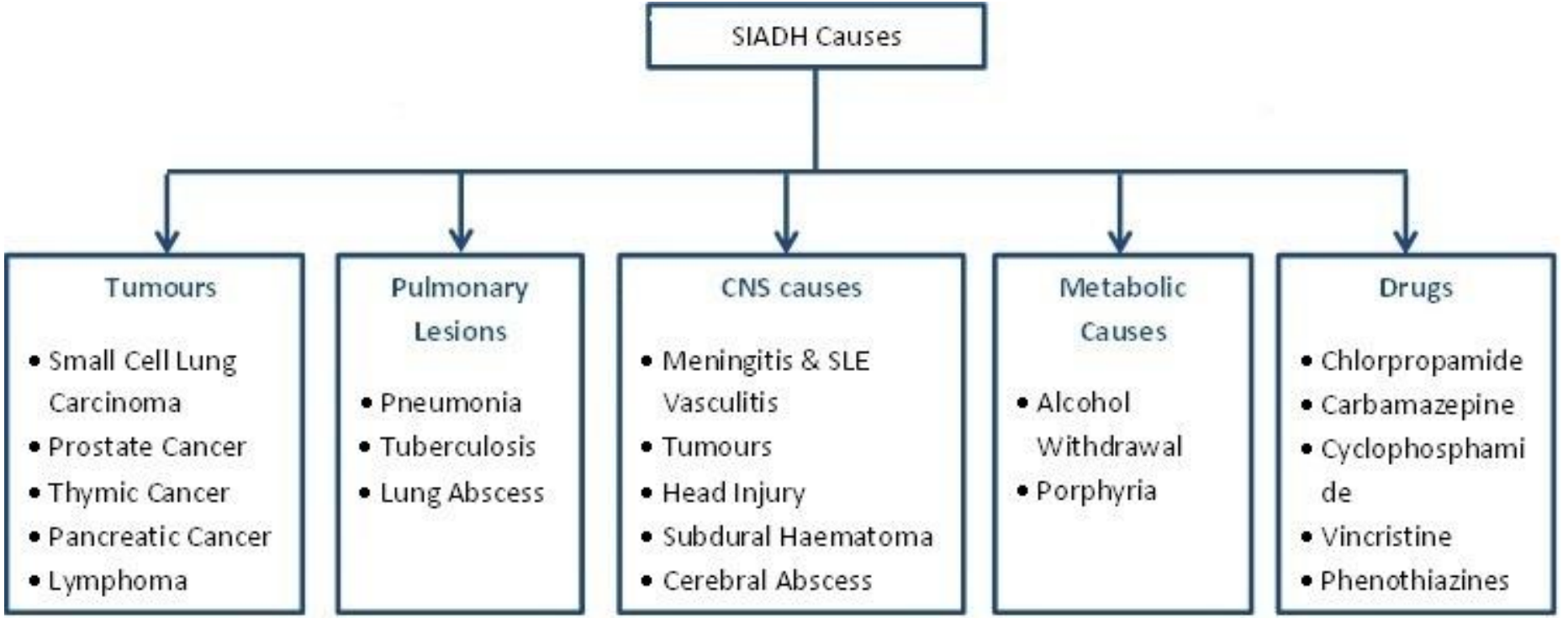
- Abnormal water load test
- Plasma vasopressin levels inappropriately elevated for the plasma osmolality

Source: Diagnostic criteria as originally defined by Bartter et al, with minor modifications

Clinical Manifestations:

- Oliguria
- Water retention
 - \uparrow CVP, \uparrow PWP
- Weight gain
- Anorexia
- Nausea & vomiting
- Muscle weakness;
muscle twitching
- Lethargy; restlessness;
confusion
- Possible seizures; coma
- Edema is rare unless
water overload > 4 L
 - Much of free-water
excess is within
cellular boundaries

SIADH Causes



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graph TD; A[SIADH Causes] --> B[Tumours]; A --> C[Pulmonary Lesions]; A --> D[CNS causes]; A --> E[Metabolic Causes]; A --> F[Drugs]; B --> B1[Small Cell Lung Carcinoma]; B --> B2[Prostate Cancer]; B --> B3[Thymic Cancer]; B --> B4[Pancreatic Cancer]; B --> B5[Lymphoma]; C --> C1[Pneumonia]; C --> C2[Tuberculosis]; C --> C3[Lung Abscess]; D --> D1[Meningitis & SLE Vasculitis]; D --> D2[Tumours]; D --> D3[Head Injury]; D --> D4[Subdural Haematoma]; D --> D5[Cerebral Abscess]; E --> E1[Alcohol Withdrawal]; E --> E2[Porphyria]; F --> F1[Chlorpropamide]; F --> F2[Carbamazepine]; F --> F3[Cyclophosphamide]; F --> F4[Vincristine]; F --> F5[Phenothiazines];
```

Tumours

- Small Cell Lung Carcinoma
- Prostate Cancer
- Thymic Cancer
- Pancreatic Cancer
- Lymphoma

Pulmonary Lesions

- Pneumonia
- Tuberculosis
- Lung Abscess

CNS causes

- Meningitis & SLE Vasculitis
- Tumours
- Head Injury
- Subdural Haematoma
- Cerebral Abscess

Metabolic Causes

- Alcohol Withdrawal
- Porphyria

Drugs

- Chlorpropamide
- Carbamazepine
- Cyclophosphamide
- Vincristine
- Phenothiazines

LEVEL 3 – SEVERE SYMPTOMS:

vomiting, seizures, obtundation,
respiratory distress, coma

hypertonic NaCl
administration, followed
by fluid restriction ± vaptan

LEVEL 2 – MODERATE SYMPTOMS:

nausea, confusion, disorientation,
altered mental status

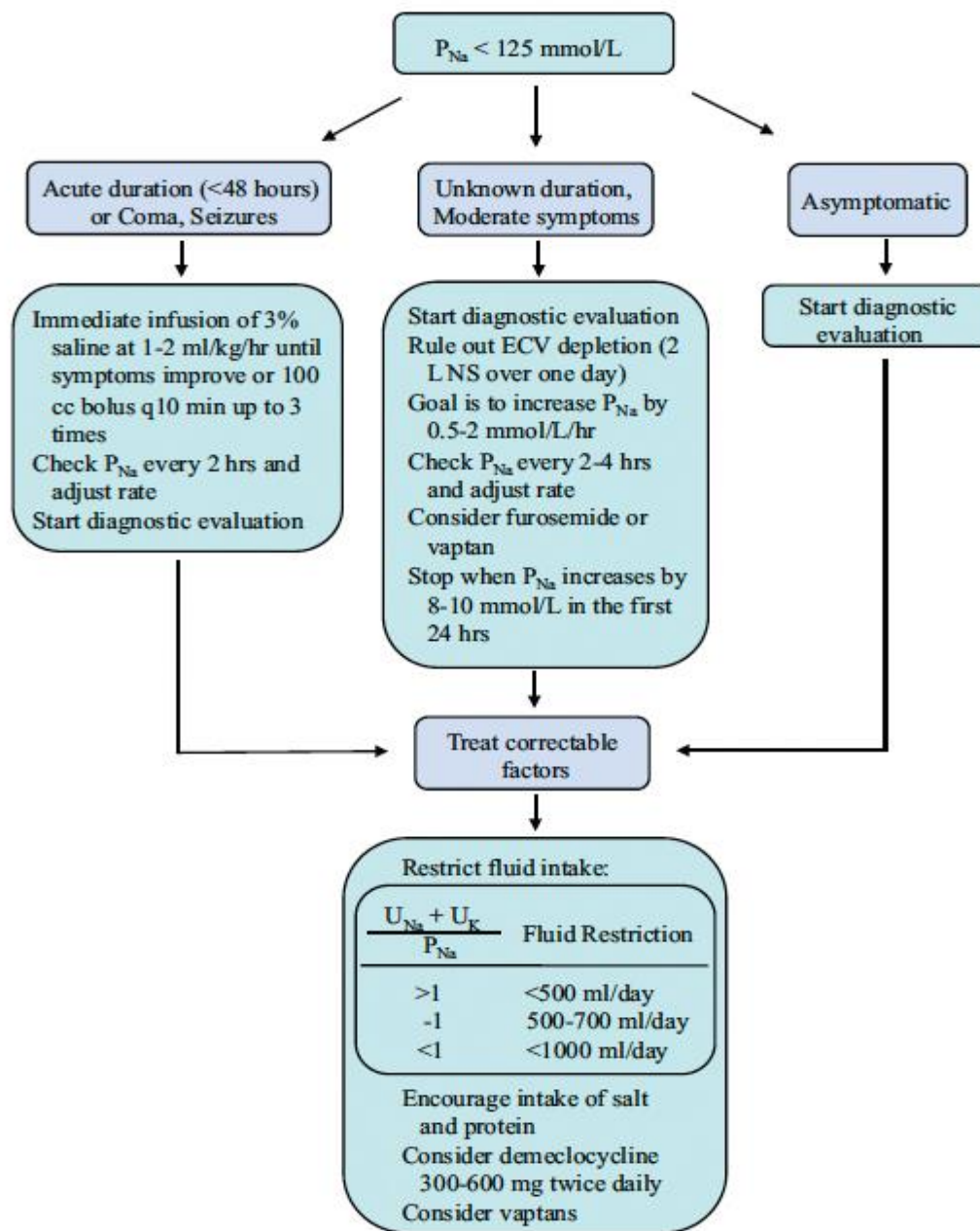
vaptan or hypertonic NaCl
administration, followed
by fluid restriction

LEVEL 1 – NO OR MINIMAL SYMPTOMS:

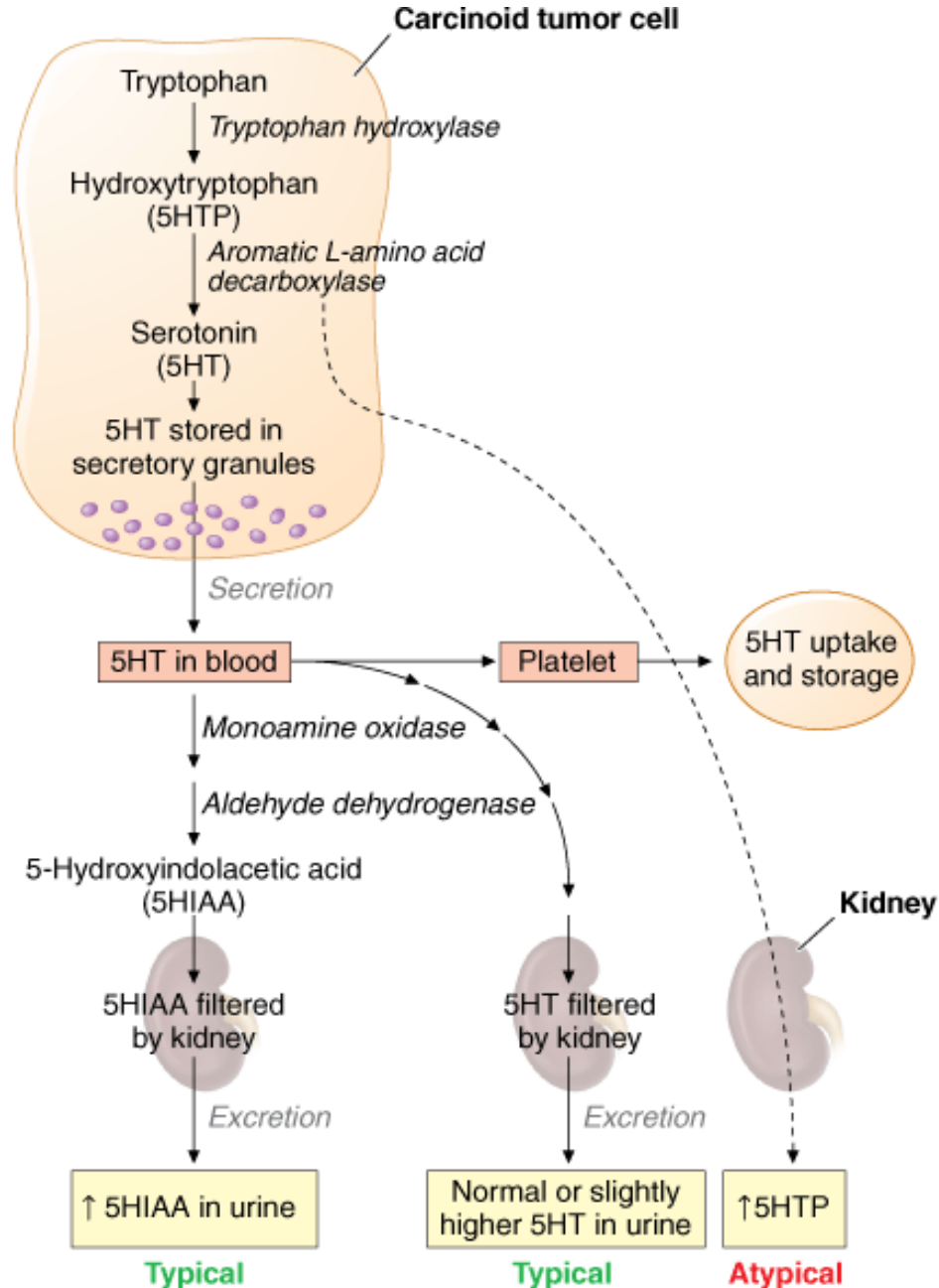
headache, irritability, inability to concentrate,
altered mood, depression

fluid restriction, but vaptan
under select circumstances:

- inability to tolerate fluid restriction or failure of fluid restriction
- very low sodium level (<125 mEq/L) with increased risk of developing symptomatic hyponatraemia
- need to correct serum [Na⁺] to safer levels for surgery or procedures, or for ICU/hospital discharge
- brain trauma with risk of worsening increased intracranial pressures
- unstable gait and/or high fracture risk
- therapeutic trial for symptom relief



P_{Na} =plasma sodium; U_{Na} =urine sodium; U_K =urine potassium.



Source: Fauci AS, Kasper DL, Braunwald E, Hauser SL, Longo DL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine*, 17th Edition: <http://www.accessmedicine.com>

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Tumour	Hormone/ Peptide	Major Symptoms
Carcinoid	Serotonin Substance P Histamine Bradykinin Kallikrein	Flushing, watery diarrhea, stomach cramps, asthma-like wheezing, heart palpita- tions, heart problems.

Carcinoid syndrome

Heart

- pulmonic and tricuspid valve thickening and stenosis
- endocardial fibrosis

Skin

- cutaneous flushes
- apparent cyanosis

Liver

- hepatomegaly

Respiratory

- cough
- wheezing
- dyspnea

Gastrointestinal

- diarrhea
- cramps
- nausea
- vomiting

retro-peritoneal and pelvic fibrosis

