East of England
ACCS Training day

Endocrine Emergencies

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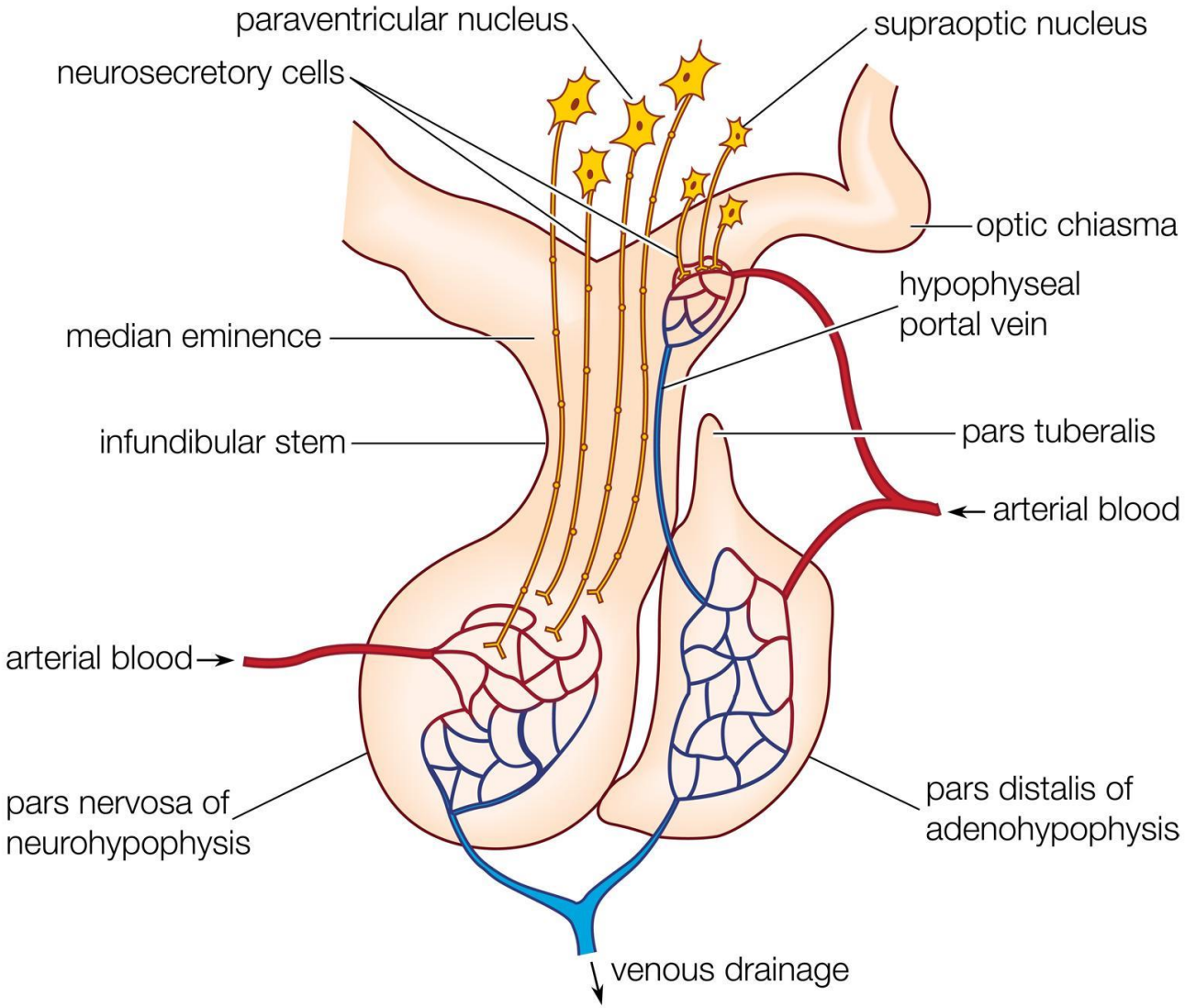


Anterior Pituitary

HGH (somatotropin) released under the influence of hypothalamic growth hormone releasing hormone (GHRH) and is inhibited by hypothalamic somatostatin

TSH released under the influence of hypothalamic thyrotropin releasing hormone TRH and inhibited by somatostatin

ACTH released under the influence of corticotropin releasing hormone

Prolactin stimulated by oxytocin, TRH, vasopressin and angiotensin 2 and inhibited by hypothalamic dopamine

Luteinizing hormone and **Follicle stimulating hormone** released under the influence of GnRH

Posterior Pituitary

ADH (vasopressin) released from the supraoptic nucleus in the hypothalamus

Oxytocin: released from the paraventricular nucleus in the hypothalamus

Oxytocin creates positive feedback loops. eg uterine contractions stimulate the release of oxytocin which in turn stimulates uterine contractions.

45yr head injury

- GCS 14/15 ---improved to 15/15
- Initial CT head normal
- Increased confusion after 24 hrs
- Repeat CT head –normal.
- What is the reason for confusion?
- What is the next test?

Investigations

- Glucose 5mmol/L
- Na 120
- K 4.5
- Renal function normal
- What further tests are required?

What other tests are to be sent to confirm the diagnosis?

SIADH

- Concentrated urine

  Ur Na >20

  Ur Osmolality >500mosmkg

- Hyponatremia

  Serum Na < 125mmol/L

  In the absence of

  hypovolemia , oedema, diuretics

How should this patient be treated and the rationale?

What is the potential life threatening complication as a result of the treatment?

SIADH

Excessive release of ADH from the posterior pituitary

Common causes: Head injury, SAH, small cell lung cancer, pneumonia, lung and brain abscess, drug induced, sarcoidosis, hypothyroidism

Hypothalamic osmoreceptors are responsible for switching off ADH production in response to a reduction in plasma osmolality

In SIADH this fails and **dilutional hyponatraemia** results

Primarily a problem with being unable to handle water loading rather than excess solute loss

Hence treatment is usually **fluid restriction**

Demeclocycline in certain cases

Diabetes insipidus

Excretion of large amounts of severely dilute urine with fluid restriction having no effect on urine concentration

Central DI: Most common
ADH deficiency

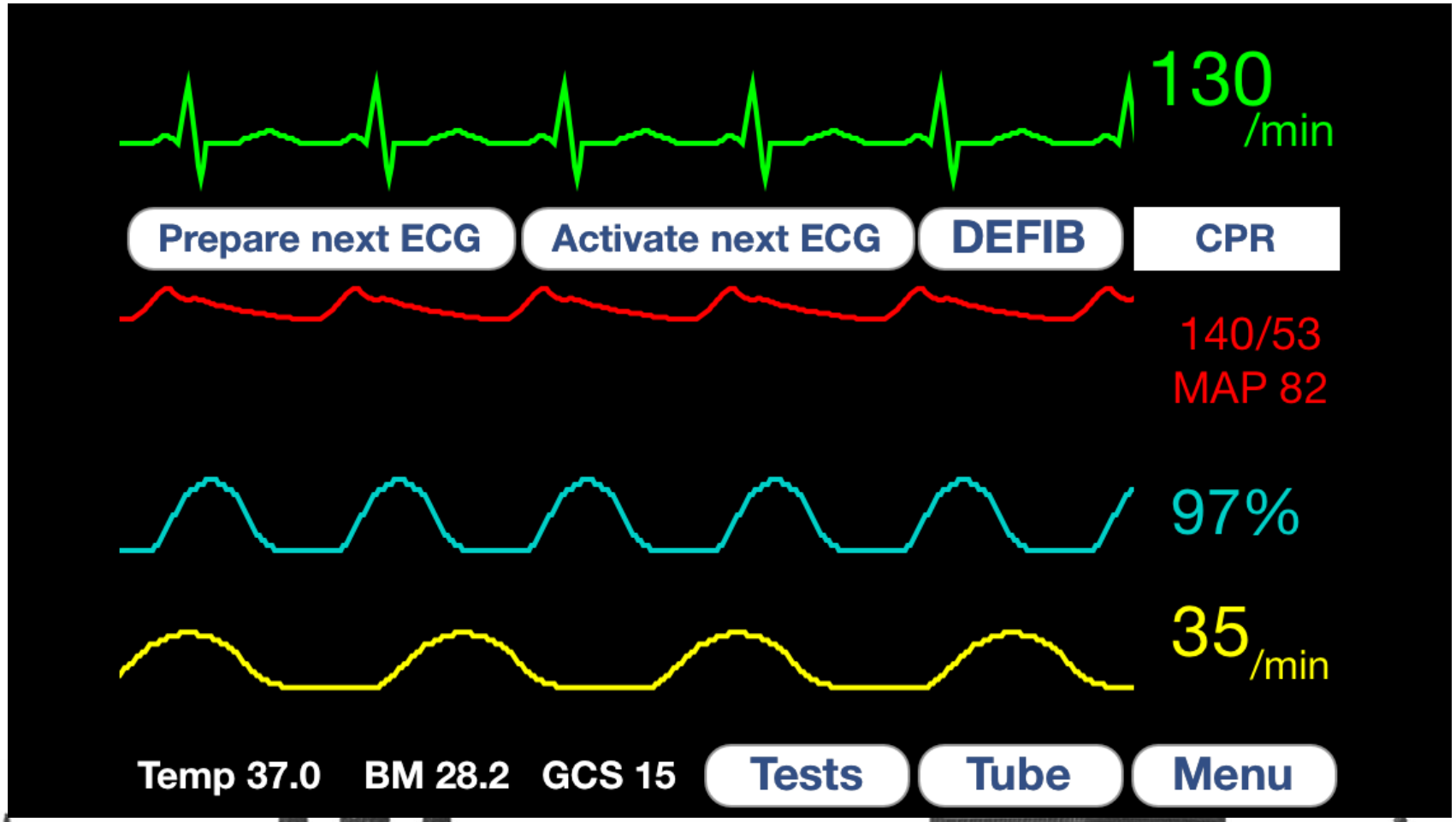
Causes: Hypoxic encephalopathy, Neurosurgery, autoimmune, pituitary tumor

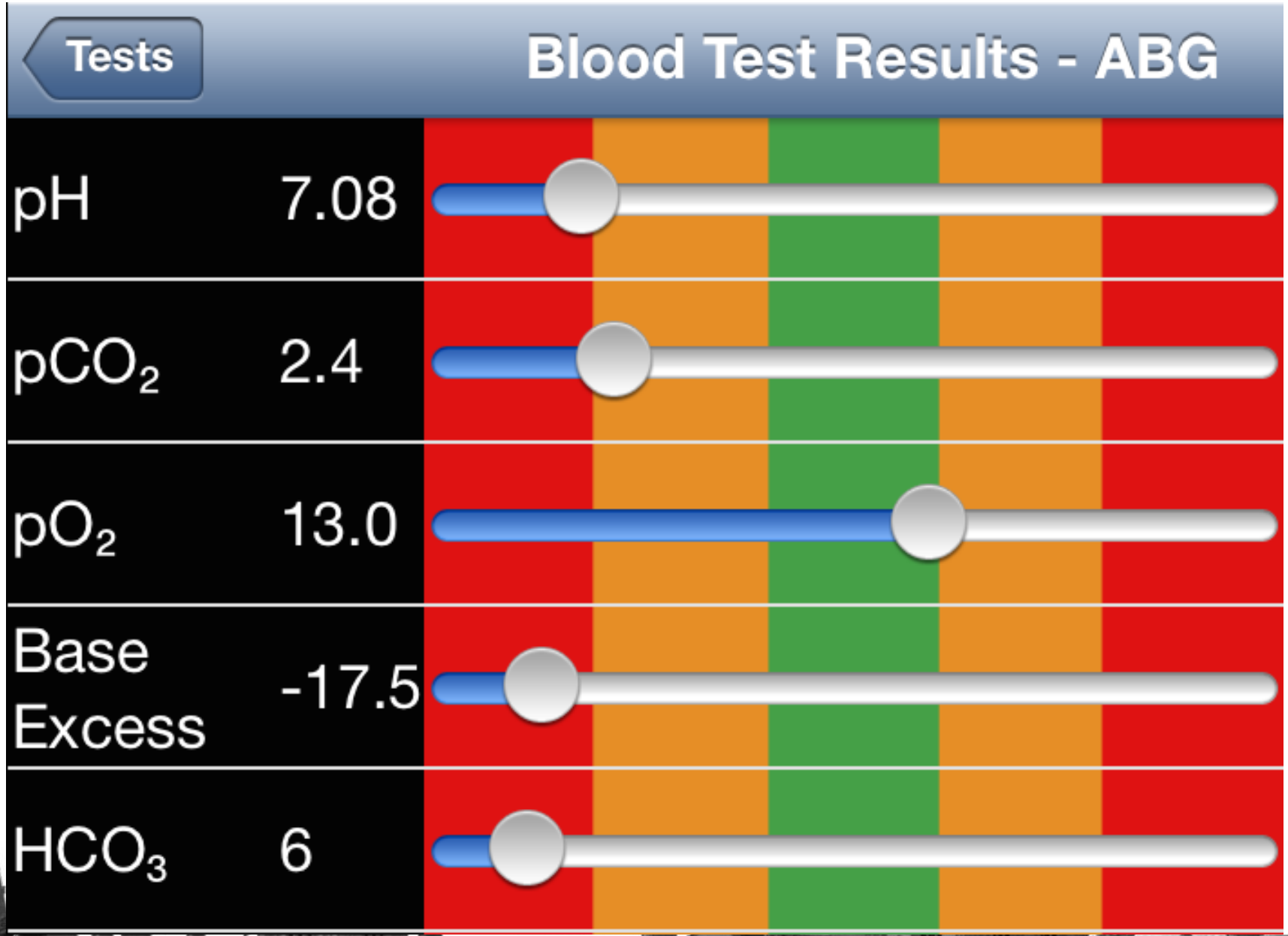
Nephrogenic DI: Lack of Aquaporin channels in the distal collecting duct

Causes: Amyloidosis, polysystic kidney disease, Lithium toxicity, hypercalcemia, hypokalaemia, release of ureteral obstruction, Sjogren syndrome, Barter syndrome, drug induced, hereditary

Diagnosis: Water deprivation test, DDAVP

16yr Male lethargic, drinking “loads”




Tests
Blood Test Results - ABG
pH
7.08
pCO2
2.4
pO2
13.0
Base Excess
-17.5
HCO3
6

Diagnostic Criteria - DKA

Ketonemia>3 mmol/L or Ketonuria > 2+ on urine dipstick

Blood glucose >11 mmol/L or known diabetes

Bicarbonate < 15 mmol/L and / or pH < 7.3

What are the indicators of severe DKA?

Indicators of Severe DKA

- Blood Ketones over 6 mmol/L
- Bicarbonate level below 5 mmol/L
- Venous/arterial pH below 7.1
- Hypokalaemia on admission (under 3.5 mmol/L)
- GCS less than 12 or abnormal AVPU scale
- Oxygen saturation below 92% on air (assuming normal baseline respiratory function)
- Systolic BP below 90 mmHg
- Pulse over 100 or below 60 bpm
- Anion gap above16

Endocrine Pancreas

Functional anatomy of the endocrine pancreas

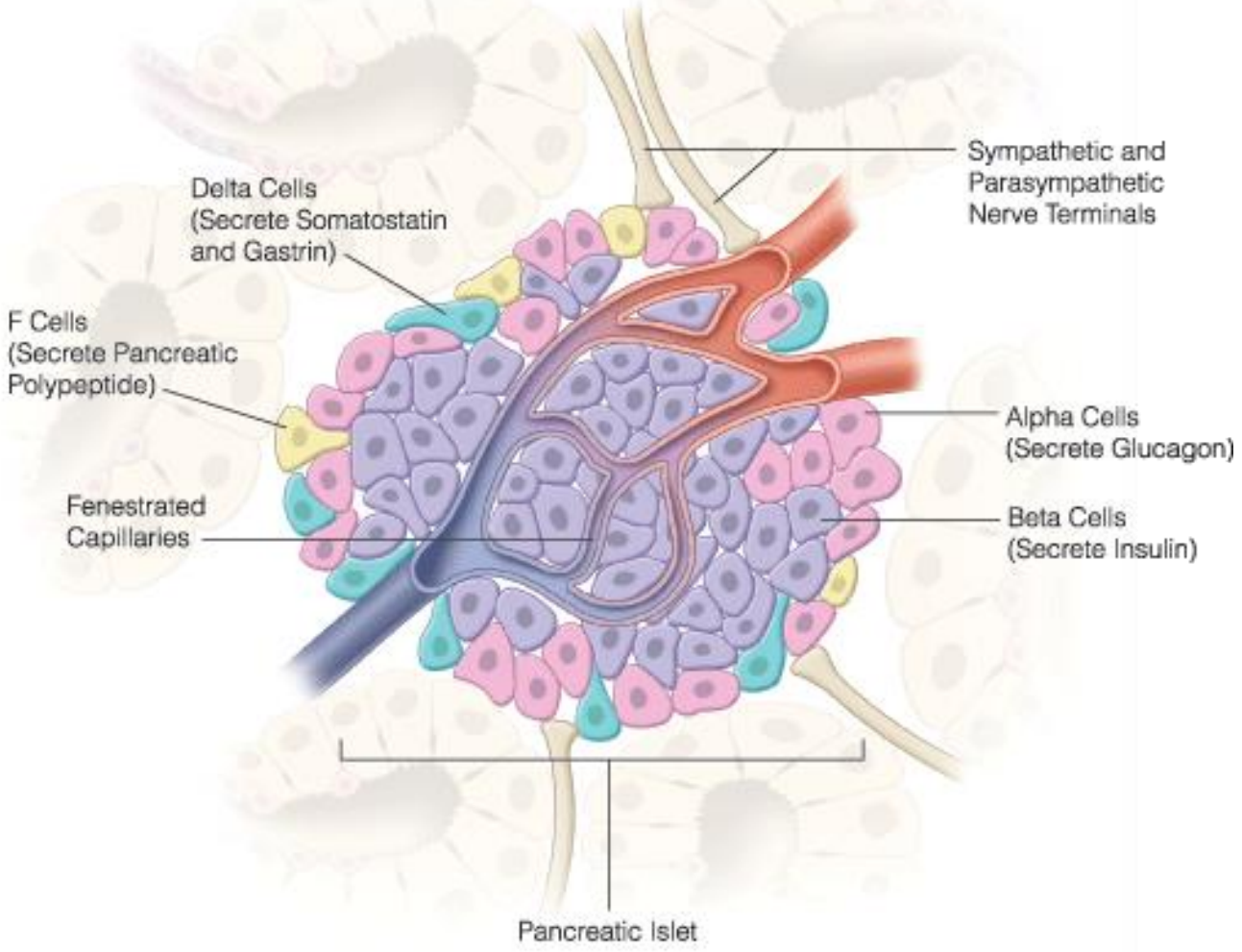
The synthesis and physiological effects of **insulin**

Glucagon: Stimulants to production and effects on the liver

Diabetes Mellitus

Physiological basis of insulin dependent and non-insulin dependent diabetes

Clinical effects of untreated diabetes


Sympathetic and
Parasympathetic
Nerve Terminals
Delta Cells
(Secrete Somatostatin
and Gastrin)
F Cells
(Secrete Pancreatic
Polypeptide)
Alpha Cells
(Secrete Glucagon)
Fenestrated
Capillaries
Beta Cells
(Secrete Insulin)
Pancreatic Islet

Insulin

Peptide hormone produced by beta cells in the pancreas

Lowers the concentration of glucose in the blood stream

Increases glycogen synthesis
Increases lipid uptake and triglyceride formation by fat cells
Increases amino acid uptake
Increases cellular potassium uptake and lowers potassium levels in the blood.

Decreases gluconeogenesis in the liver

Glucagon

Peptide hormone produced by **alpha cells** of the pancreas

Raises concentration of glucose in the bloodstream

Binds to **glucagon receptor** on hepatocytes

Promotes **gluconeogenesis** and **glycogenolysis**

Glucagon **turns off glycolysis** in the liver

Induces lipolysis yielding **glycerol** and free fatty acids

Treatment aims of DKA

- Restoration of circulating volume
- Potassium replacement
- Commence a fixed rate intravenous insulin infusion 0.1 Unit/kg/hr
- Identify and treat precipitating factors
- Achieve a rate of fall of ketones of at least 0.5 mmol/L/hr
- In the absence of ketone measurement, bicarbonate should rise by 3 mmol/L/hr
- Thromboprophylaxis-LMWH

Fluid	Volume
0.9% sodium chloride 1L *	1000ml over 1st hour
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 2 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 4 hours
0.9% sodium chloride 1L with potassium chloride	1000ml over next 6 hours
Re-assessment of cardiovascular status at 12 hours is mandatory, further fluid may be required	

*Potassium chloride may be required if more than 1 litre of sodium chloride has been given already to resuscitate hypotensive patients

Potassium level in first 24 hours (mmol/L)	Potassium replacement in mmol /L of infusion solution
Over 5.5	Nil
3.5-5.5	40
Below 3.5	Senior review as additional potassium needs to be given (see serious complications section)

75 yrs known DM-2
SOB and fever
capillary Blood gluscose-35
urea 13
Na 155
K 4

Calculate Osmolarity in this patient

Osmolarity

Calculated serum Osmolarity = 2(Na+K)+urea+glucose

Osmolar Gap = calculated – measured (lab)

Usually < 10 mosmol/kg

Treatment of HHS

- Similar to DKA
- Be careful with fluids speeds as most patients are elderly
- If Na > 155 , use half normal saline

26 Female has wisdom tooth extracted yesterday and today feeling lethargic and “fainty”

PR 130/m

BP90/40 mmHg

SaO2 96% poor trace

RR 24/m

Na 126

K 6

Ur 10.9

Cr 115

Ph 7.27

PO2 12 kpa

PCO2 3 kpa

HCO3 12

BE -10

What other tests do you send and what is the rationale?

Tests to differentiate primary and secondary Addison's

- Serum Cortisol
- Serum ACTH

Treatment

- Rehydration
- Hydrocortisone /Dexamethasone
- No need of fludocortisone in ED
- Correct hypoglycemia and hyperkalemia
- Treat the trigger

Adrenal insufficiency

Addison's disease (chronic hypoadrenalism)

Causes:

Adrenal dysgenesis
Impaired steroidogenesis (CAH, Smith-Lemli-Opitz syndrome)
Adrenal destruction (autoimmune adrenalitis - isolated or part of autoimmune polyendocrine syndrome - APS)
Corticosteroid withdrawal - exogenous glucocorticoids suppress CRH and ACTH

Fatigue, postural dizziness, weight loss, anxiety, nausea, diarrhoea, headache, salt craving
Low blood pressure
Hyperpigmentation of the skin
(ACTH is a precursor for Melanocyte stimulating hormone)

Adrenal Gland

Functional anatomy

Cortical function

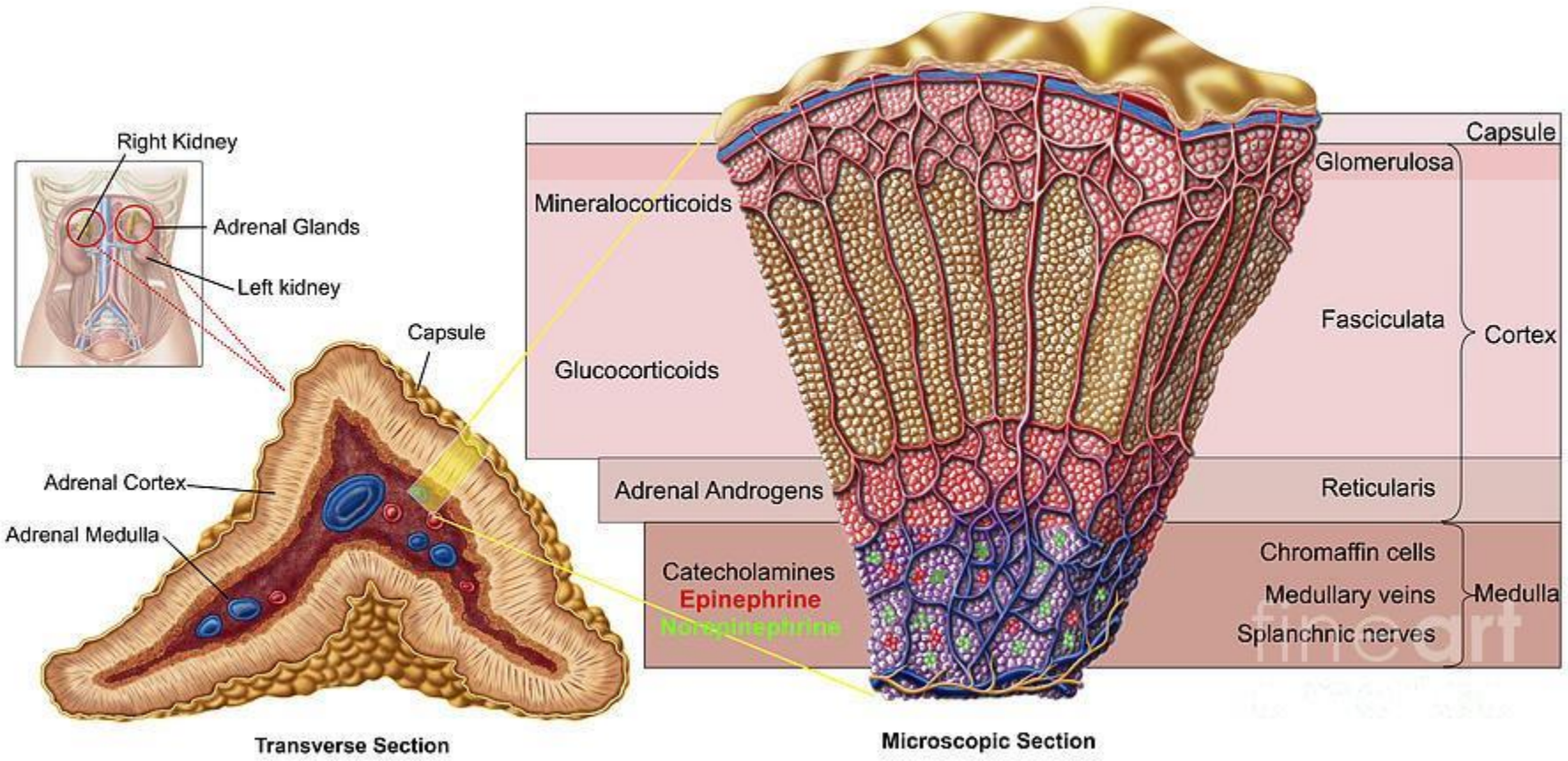
Effects of glucocorticoids

Clinical effects of disordered glucocorticoid secretion

Medullary function

Adrenaline

Clinical effects of disordered medullary function


Right Kidney
Adrenal Glands
Left kidney
Capsule
Adrenal Cortex
Adrenal Medulla
Transverse Section
Capsule
Glomerulosa
Mineralocorticoids
Fasciculata
Glucocorticoids
Cortex
Adrenal Androgens
Reticularis
Chromaffin cells
Catecholamines
Epinephrine
Norepinephrine
Medullary veins
Medulla
Splanchnic nerves
Microscopic Section

Cortisol

A steroid hormone

- **It acts to prepare the body for stress**

Cortisol causes an **increase in all gluconeogenisis enzymes**

Cortisol increases the production of amino acids from muscle breakdown. **It halts the synthesis of protein and fat**

Glucocorticoids reproduce glucagon action and oppose insulin action

- **Suppresses the immune system**:

- **Decreases bone formation by**:

Direct inhibition of osteoblast function
Inhibit gastrointestinal calcium absorption

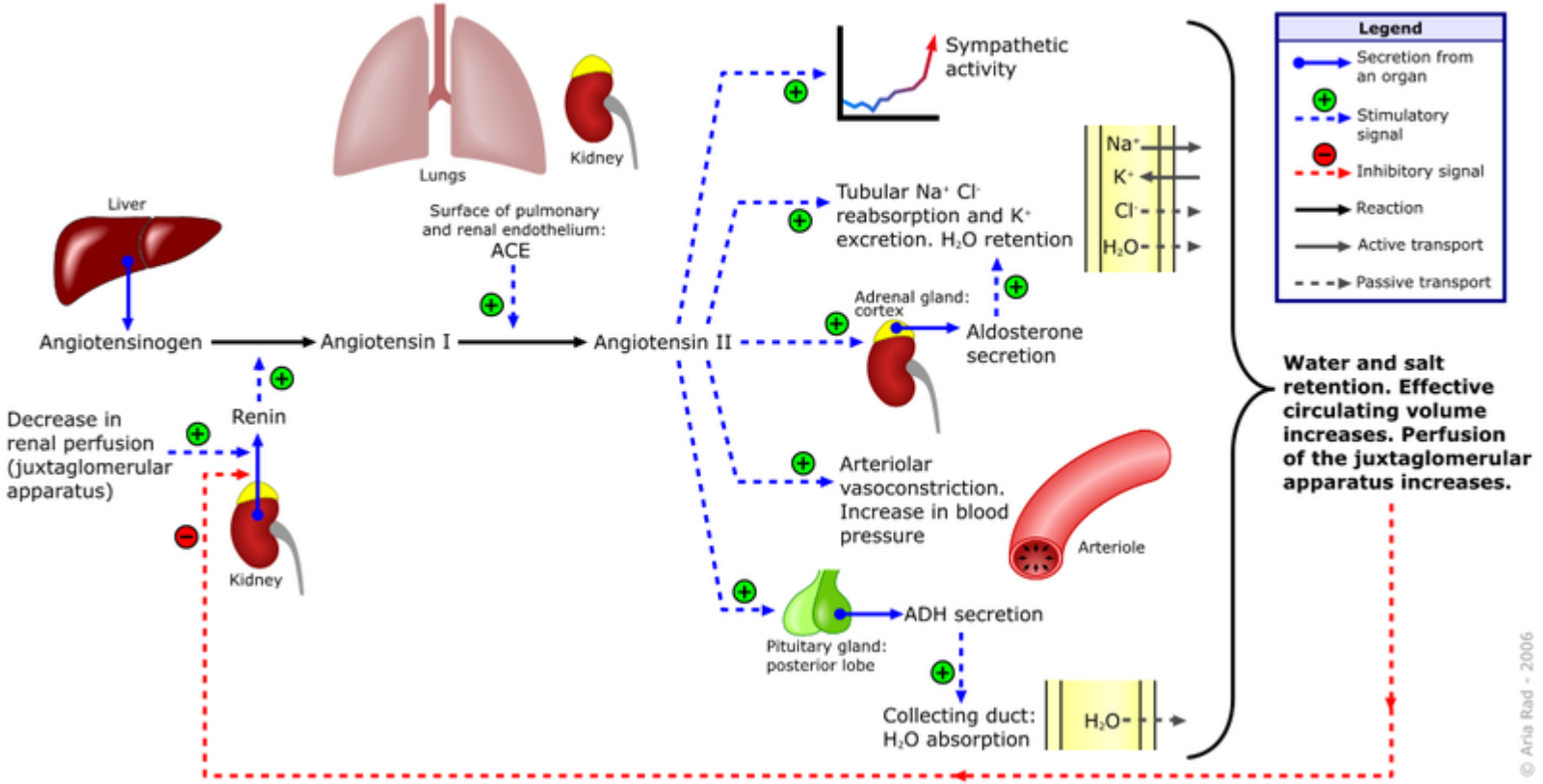
Cushing’s syndrome

Prolonged exposure to inappropriately high levels of cortisol

Rapid weight gain
Irritability, depression
Bone and muscle weakness
Diabetes mellitus
Hypertension
Amenorrhea in women
Decreased fertility in men
Hirsutism
Baldness
Hypercholesterolaemia

Dexamethasone suppression test

Renin-angiotensin-aldosterone system



Phaeochromocytoma

Neuroendocrine tumor of the adrenal medulla

Excess catecholamines

Elevated heart rate, blood pressure with orthostatic hypotension
Paliptations, anxiety, diaphoresis
Weight loss
Elevated blood glucose (due to catecholamine induced lipolysis, high circulating free fatty acids and subsequent inhibition of glucose uptake by muscle)

25% familial, also a feature of MEN II syndrome

Measurements of catecholamines and metanephrines in plasma and urine

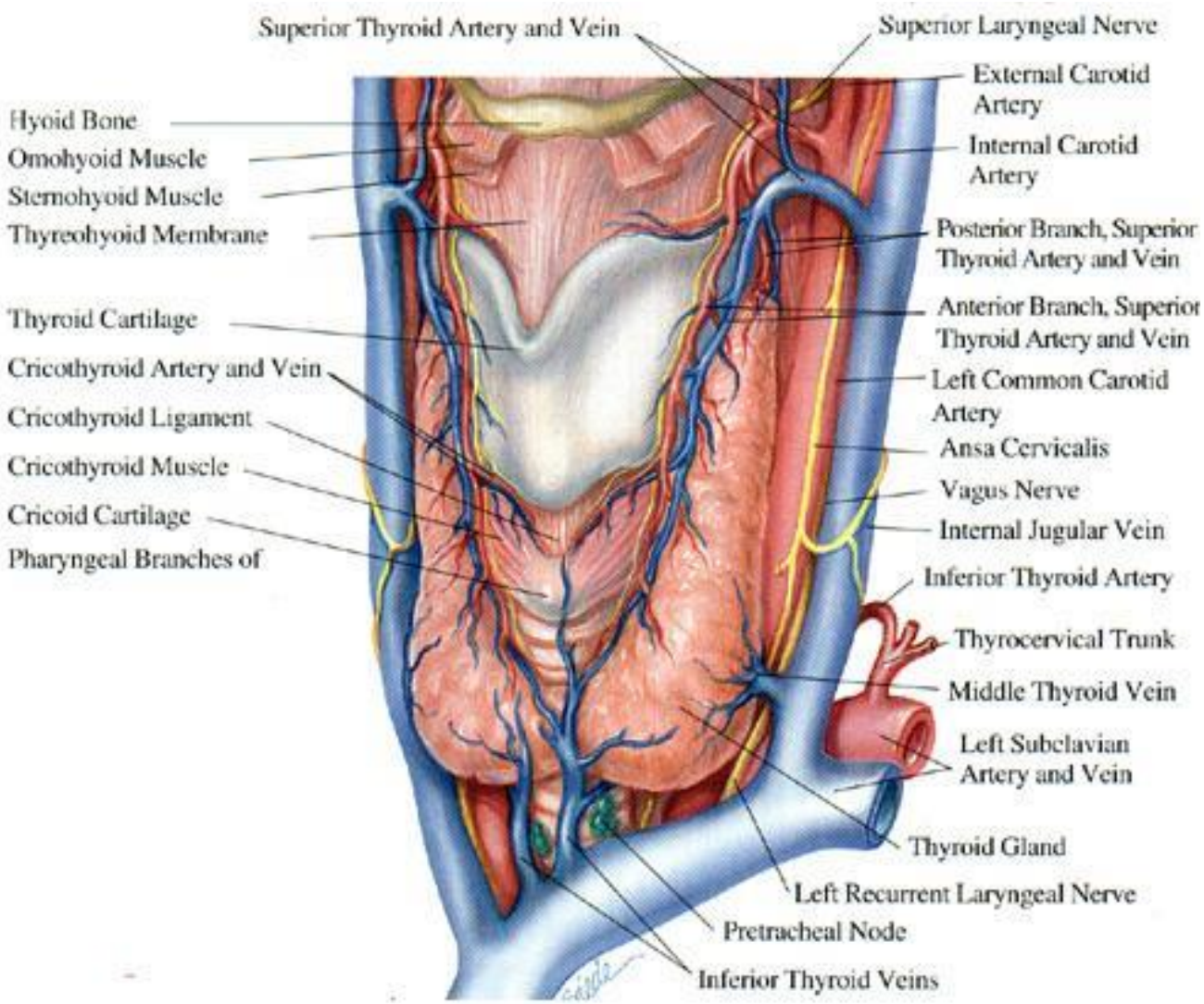
Thyroid Physiology

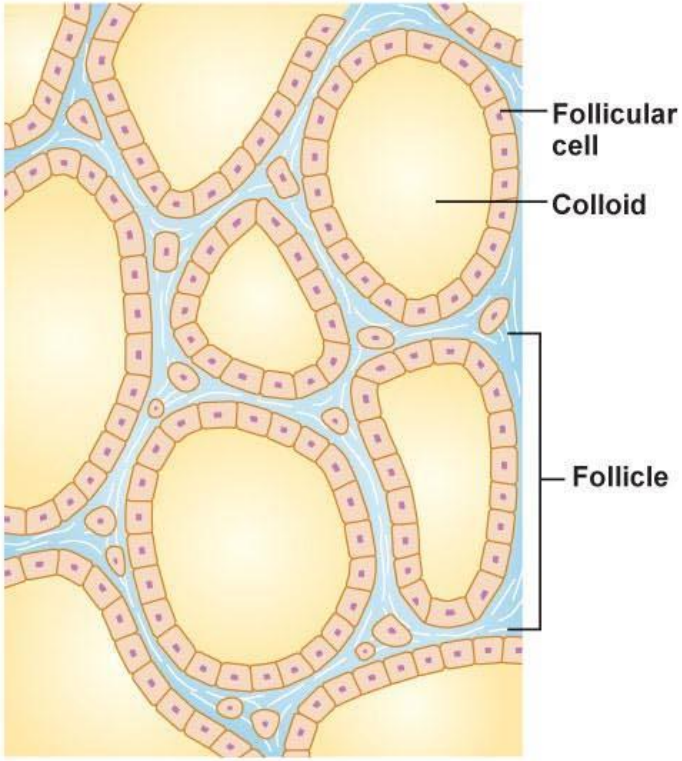
Functional anatomy

Transport of thyroid hormones

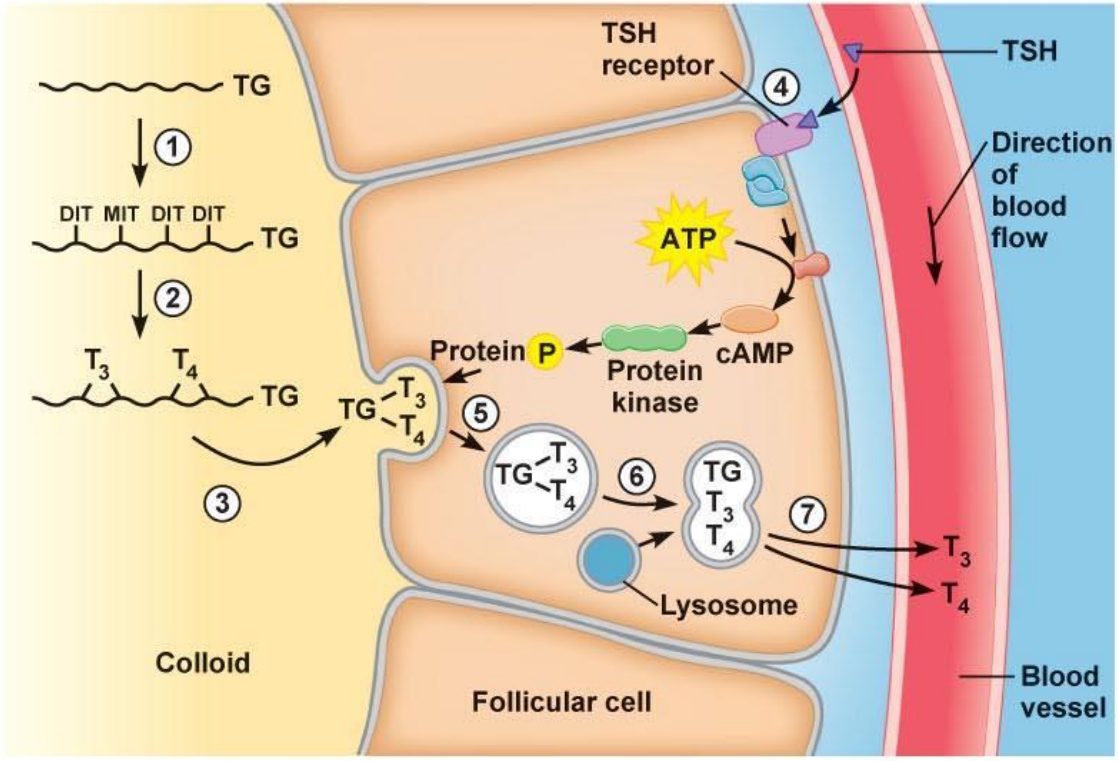
Physiological effects of thyroid hormones

Effects of disordered function

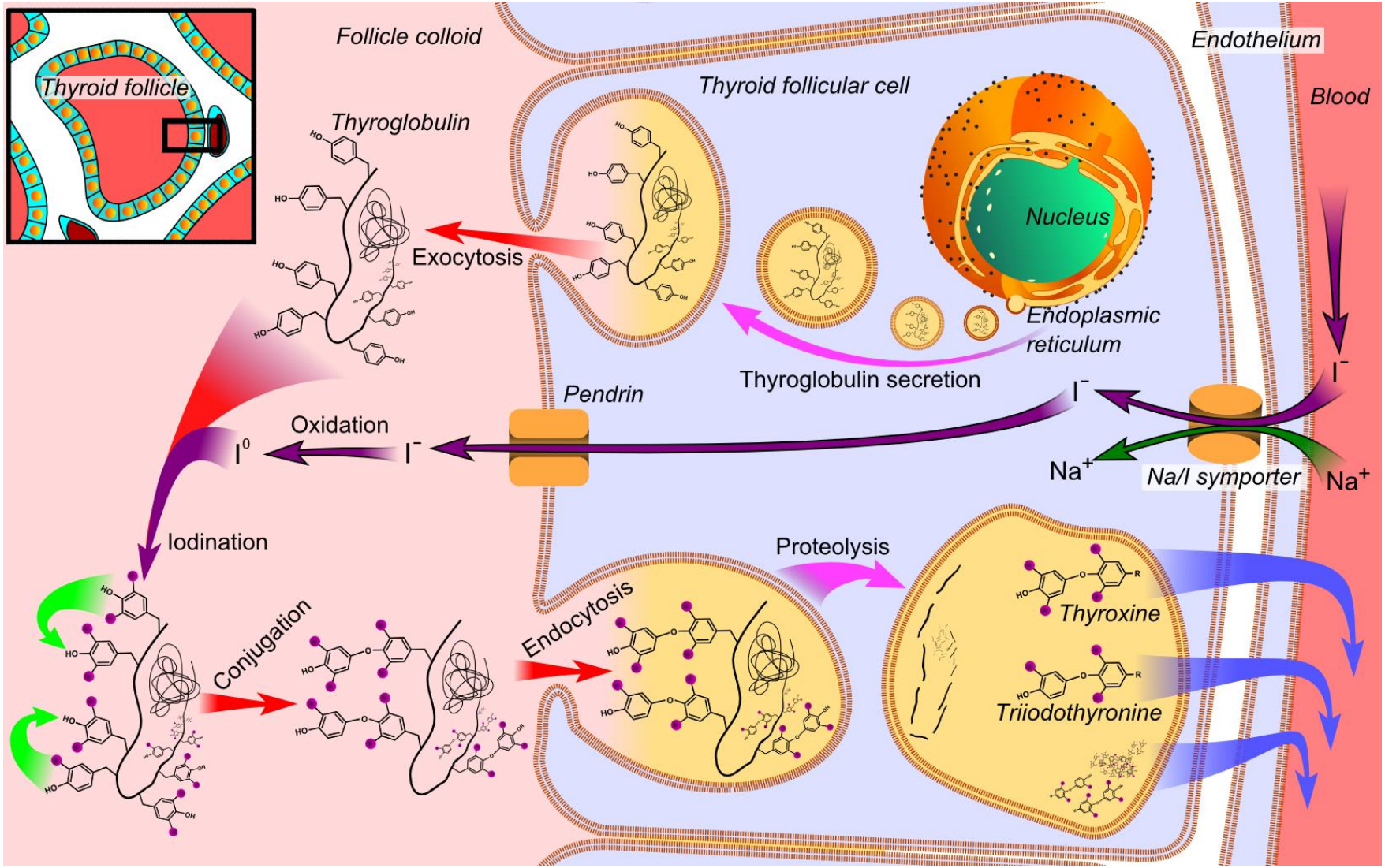

Superior Thyroid Artery and Vein
Superior Laryngeal Nerve
External Carotid Artery
Internal Carotid Artery
Hyoid Bone
Omohyoid Muscle
Sternohyoid Muscle
Thyreohyoid Membrane
Posterior Branch, Superior Thyroid Artery and Vein
Anterior Branch, Superior Thyroid Artery and Vein
Thyroid Cartilage
Cricothyroid Artery and Vein
Cricothyroid Ligament
Cricothyroid Muscle
Cricoid Cartilage
Pharyngeal Branches of
Left Common Carotid Artery
Ansa Cervicalis
Vagus Nerve
Internal Jugular Vein
Inferior Thyroid Artery
Thyrocervical Trunk
Middle Thyroid Vein
Left Subclavian Artery and Vein
Thyroid Gland
Left Recurrent Laryngeal Nerve
Pretracheal Node
Inferior Thyroid Veins



(a) Thyroid follicles



(b) Synthesis and secretion of thyroid hormones


Thyroid follicle
Follicle colloid
Thyroglobulin
Exocytosis
Thyroid follicular cell
Endothelium
Blood
Nucleus
Endoplasmic reticulum
Thyroglobulin secretion
Pendrin
Oxidation
I^0
I^-
I^-
I^-
Na^+
Na^+
Na/I symporter
Iodination
Conjugation
Endocytosis
Proteolysis
Thyroxine
Triiodothyronine

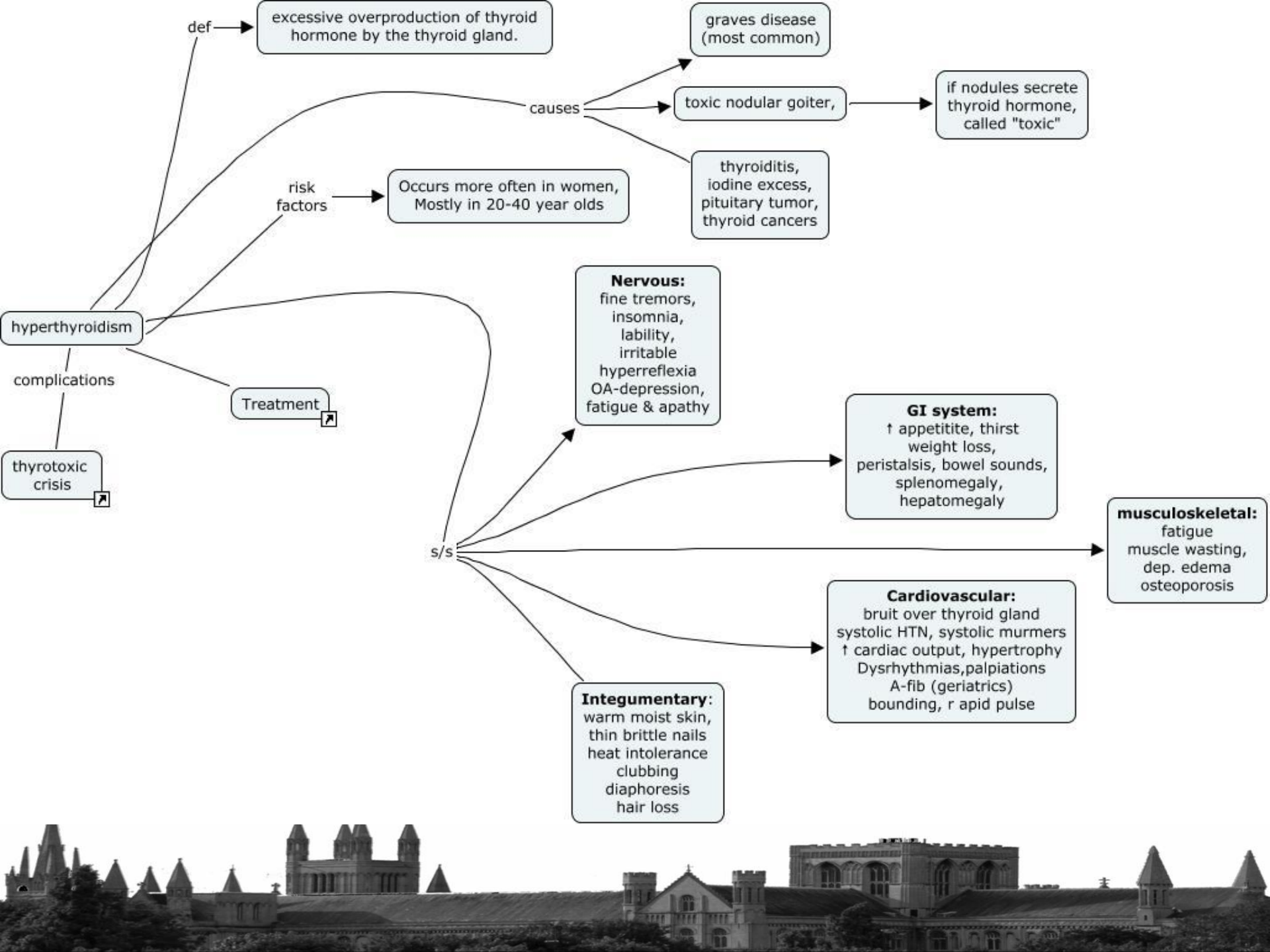

def
excessive overproduction of thyroid hormone by the thyroid gland.
causes
graves disease (most common)
toxic nodular goiter,
if nodules secrete thyroid hormone, called "toxic"
thyroiditis, iodine excess, pituitary tumor, thyroid cancers
risk factors
Occurs more often in women, Mostly in 20-40 year olds
hyperthyroidism
complications
Treatment
thyrotoxic crisis
s/s
Nervous: fine tremors, insomnia, lability, irritable hyperreflexia OA-depression, fatigue & apathy
GI system: ↑ appetitite, thirst weight loss, peristalsis, bowel sounds, splenomegaly, hepatomegaly
musculoskeletal: fatigue muscle wasting, dep. edema osteoporosis
Cardiovascular: bruit over thyroid gland systolic HTN, systolic murmers ↑ cardiac output, hypertrophy Dysrhythmias,palpiations A-fib (geriatrics) bounding, r apid pulse
Integumentary: warm moist skin, thin brittle nails heat intolerance clubbing diaphoresis hair loss

TABLE 2: WHAT CAUSES HYPOTHYROIDISM?

Several factors may contribute to the development of hypothyroidism, including:

Hashimoto's disease
Thyroiditis, or inflammation of the thyroid gland
Congenital hypothyroidism, or hypothyroidism that is present at birth
Surgical removal of part or all of the thyroid gland
Radiation treatment of the thyroid
Use of certain pharmacologic agents, such as amiodarone, interferon-alpha, lithium, interleukin-2

Adapted from references 2-4 and 6.

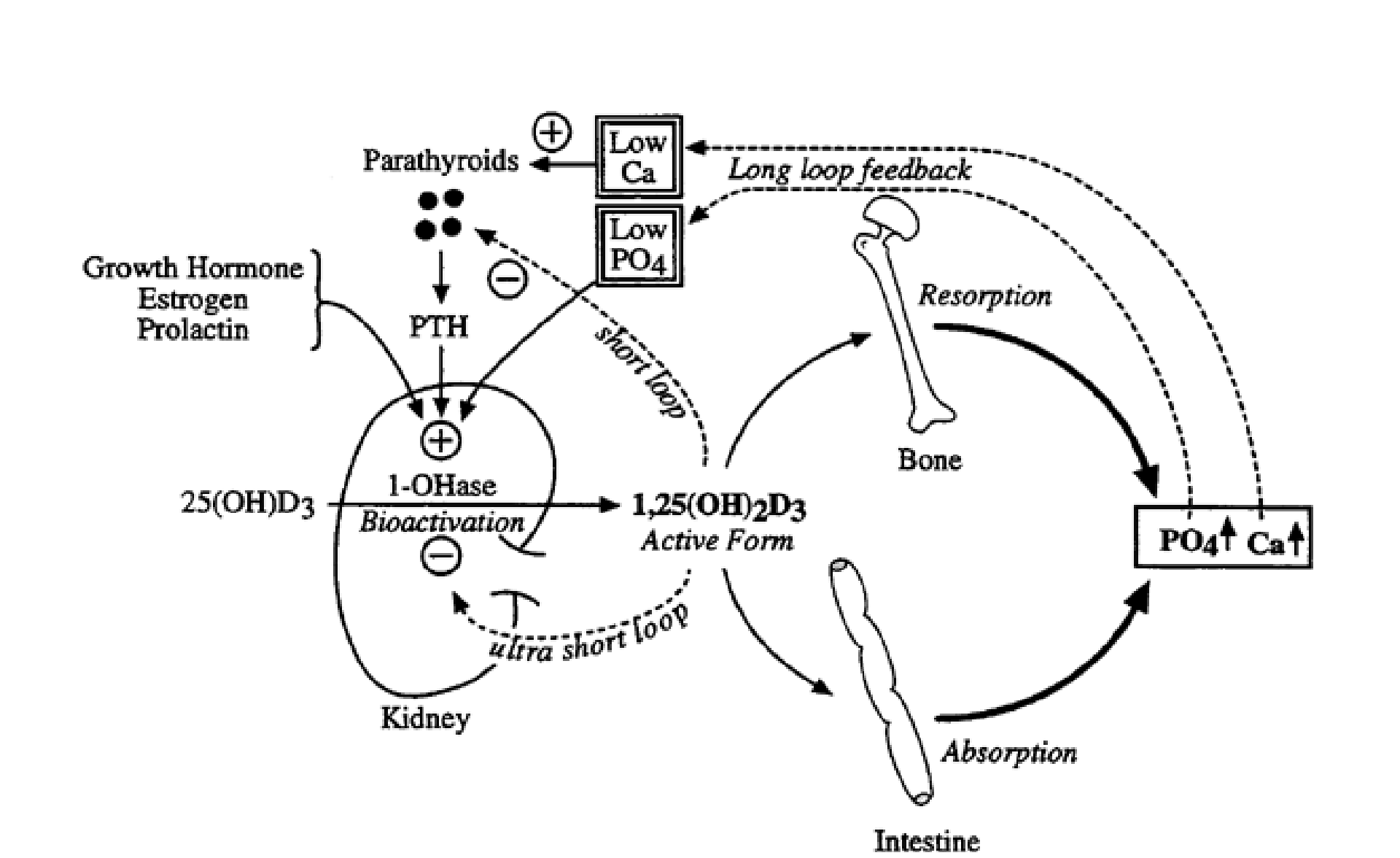
Calcium and Bone Physiology

Functions of Calcium in health

Transportation of Calcium

PTH, Calcitonin and Vitamin D3

Effects of disordered calcium physiology


Parathyroids
Low Ca
Low PO4
Long loop feedback
Growth Hormone
Estrogen
Prolactin
PTH
short loop
Resorption
Bone
1-OHase
Bioactivation
25(OH)D3
1,25(OH)2D3
Active Form
PO4↑ Ca↑
ultra short loop
Kidney
Absorption
Intestine

85yr is found to be off legs
PR 100 ; BP100/60

Na 147
K 5
Ur 9
Cr 150

Ph 7.36

HCO3 23

PCO2 4Kpa

What is the provisional diagnosis?

How to detect AKI?

Detect AKI using (p)RIFLE, AKIN, KDIGO criteria:	
Serum creatinine	rise ≥ 26 micromol/litre from baseline within 48 hours
Serum creatinine	rise by 50% or more in 7 days
Urine output	< 0.5ml/kg body weight/hour for 6 consecutive hours in adults

What are the risk factors for AKI?

Risk factors: adults

- Chronic kidney disease (or history of)
- Diabetes
- Heart failure
- Sepsis
- Hypovolaemia
- Age 65 years or over
- Use of drugs with nephrotoxic potential (for example, NSAIDs, ACE inhibitors)
- Use of iodinated contrast agents within past week
- Oliguria
- Liver disease
- Limited access to fluids, e.g. via neurological impairment
- Deteriorating early warning scores
- Symptoms or history of urological obstruction

References

http://chemistry.gravitywaves.com/CHE452/20_Calcium%20Homeostasis16.htm
http://en.wikipedia.org/wiki/Glucocorticoid_remediable_aldosteronism
http://en.wikipedia.org/wiki/Thyroid_hormone
http://www.evergreensurgical.com/articles/Thyroid2.html
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http://www.sciamsurgery.com/sciamsurgery/institutional/figTabPopup.action?bookId=ACS&linkId=part11_ch09_fig16&type=fig
http://kids.britannica.com/elementary/art-48974/The-anatomy-of-the-mammalian-pituitary-gland-showing-the-anterior
http://diabetes.diabetesjournals.org/content/55/Supplement_2/S9/F1.large.jpg