DIABETES AND ENDOCRINOLOGY

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CTF and Diabetes &Endocrinology SpR

Barts Health

WHAT DO YOU NEED TO KNOW ABOUT DIABETES FOR FINALS?

- Classification of diabetes
- Management of diabetes
- Complications of diabetes
- Diabetes emergencies

WHAT DO YOU NEED TO KNOW ABOUT DIABETES FOR FINALS?

- ~~Classification of diabetes~~
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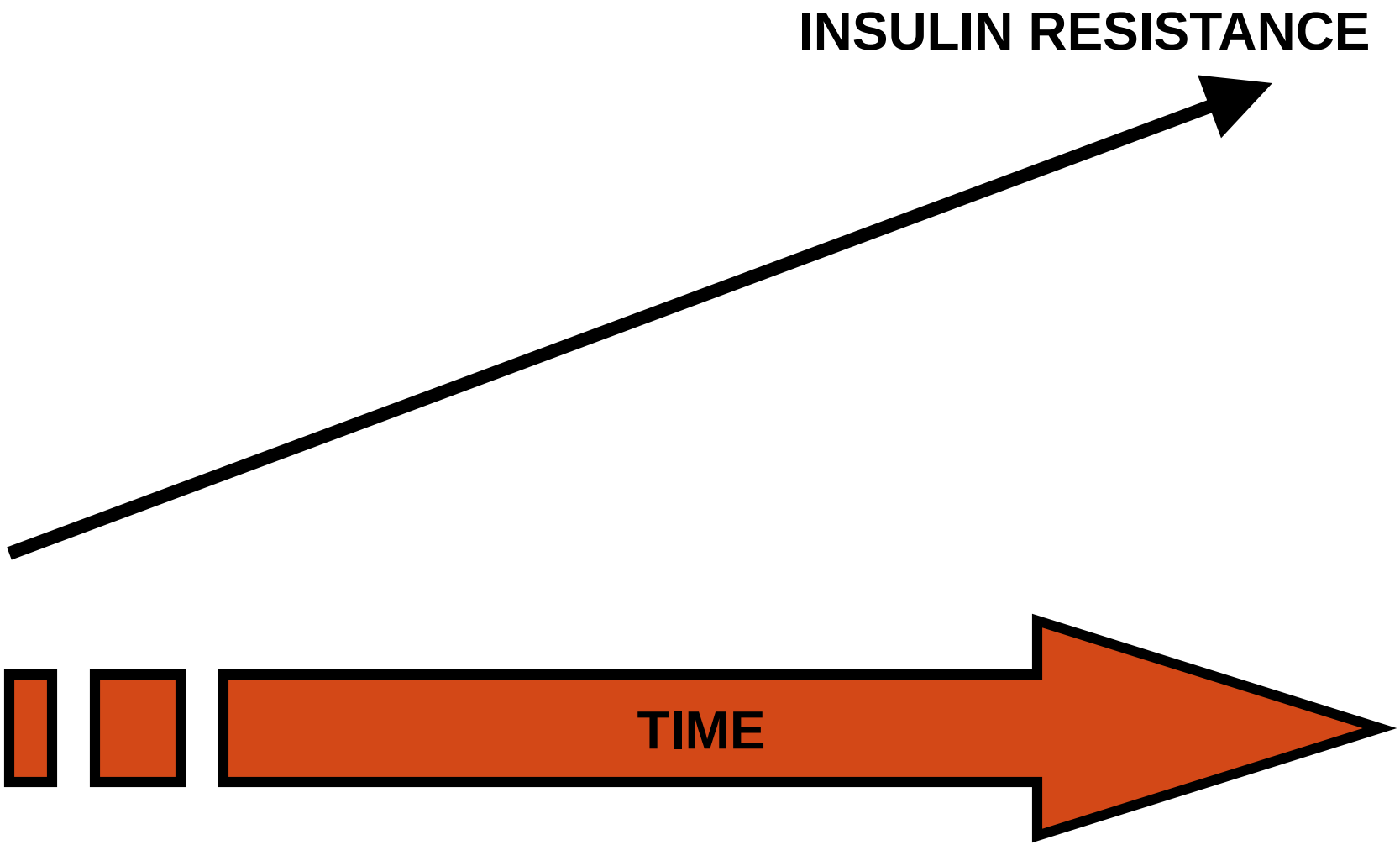
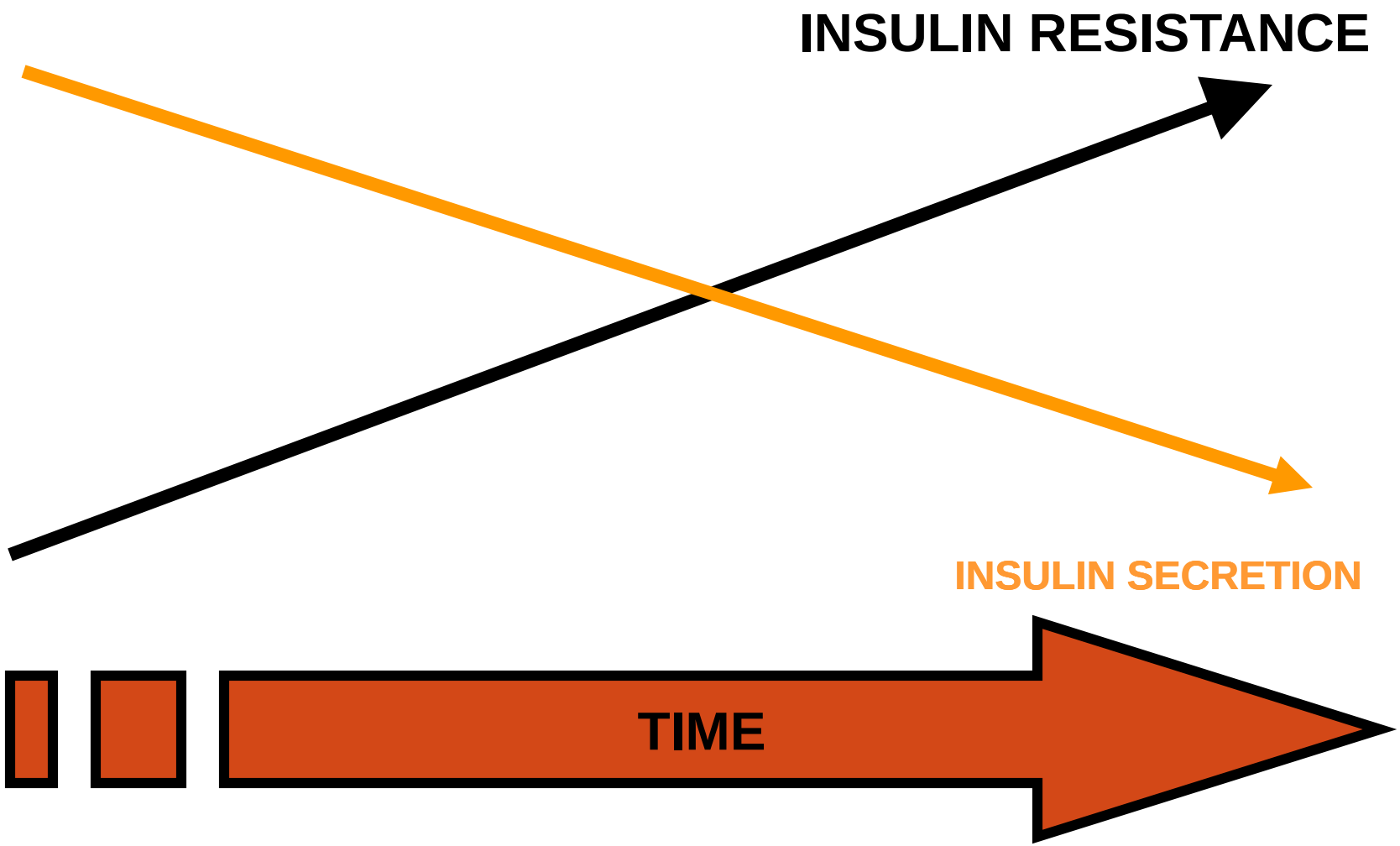
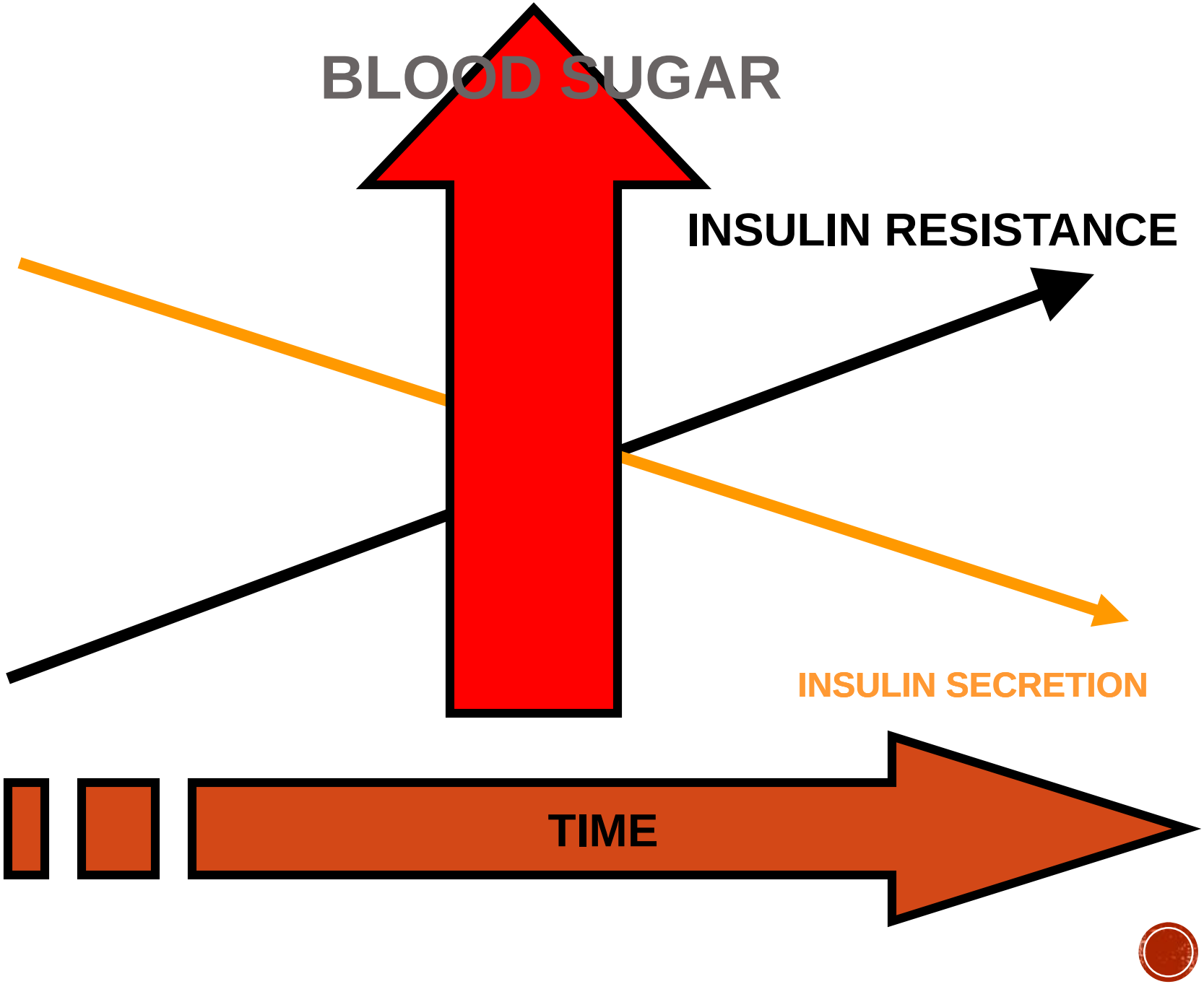
CLASSIFICATION

- Type 1 Diabetes; *"absolute insulin deficiency"*
- Type 2 Diabetes; *"insulin resistance => deficiency"*


INSULIN RESISTANCE
TIME


INSULIN RESISTANCE
INSULIN SECRETION
TIME


BLOOD SUGAR
INSULIN RESISTANCE
INSULIN SECRETION
TIME

CLASSIFICATION

- Type 1 Diabetes; *"absolute insulin deficiency"*
- Type 2 Diabetes; *"insulin resistance => deficiency"*
- Other
  - Pancreatic disease
    - *Pancreatitis / pancreatectomy*
  - Genetic disease
    - *Cystic Fibrosis / Haemochromatosis*
  - Gestational Diabetes

WHAT DO YOU NEED TO KNOW ABOUT DIABETES FOR FINALS?

- ~~Classification of diabetes~~
- ~~Management of diabetes~~
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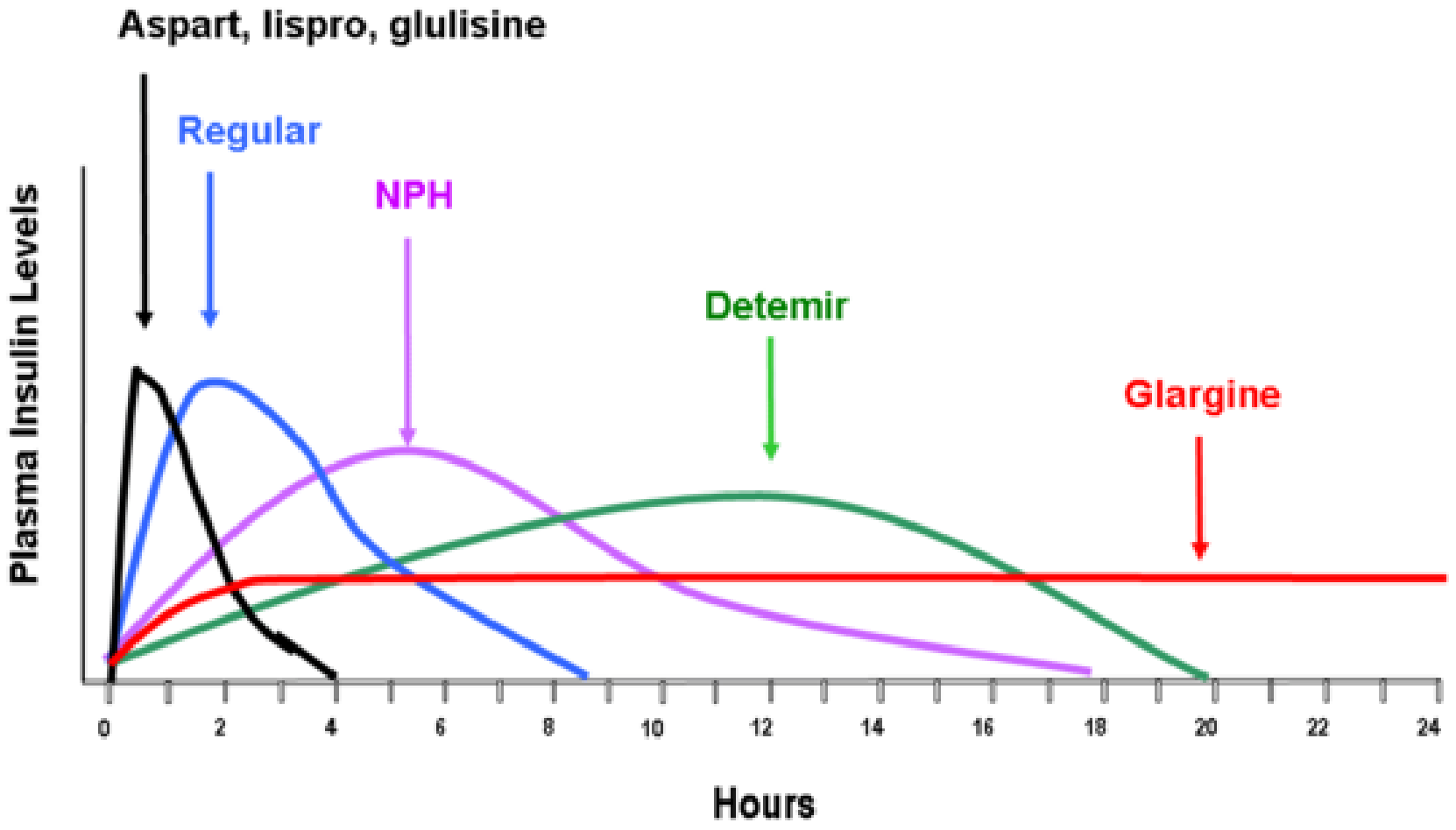
MANAGEMENT OF T1DM

- ??

MANAGEMENT OF T1DM

- Insulin!

INSULIN - PROFILES OF ACTION



MANAGEMENT OF T2DM

- Diet and exercise
- Insulin sensitiser
- Insulin secretagogue
- Reduce food absorption
- Increase glucose loss

- Insulin

WHAT DO YOU NEED TO KNOW ABOUT DIABETES FOR FINALS?

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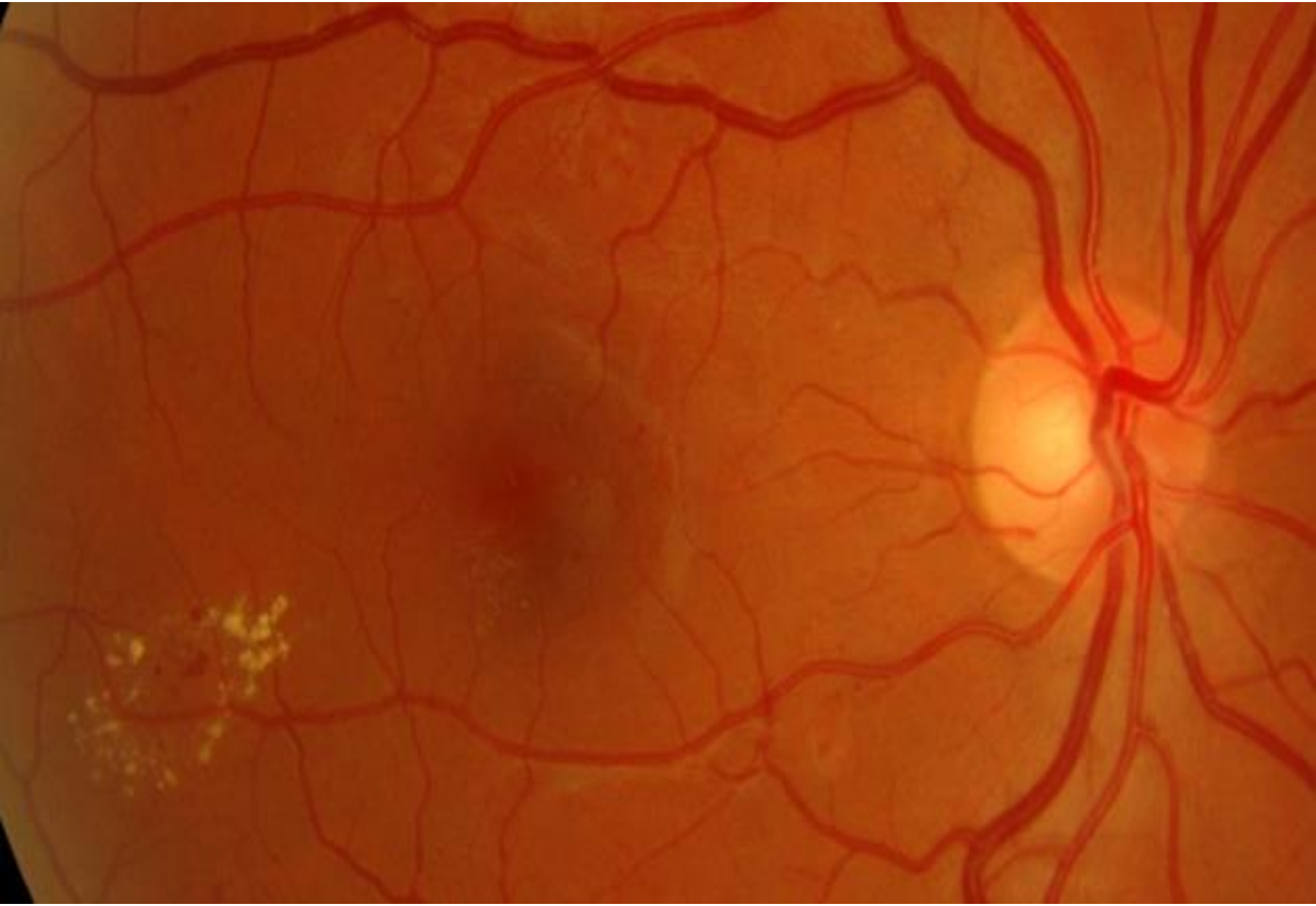
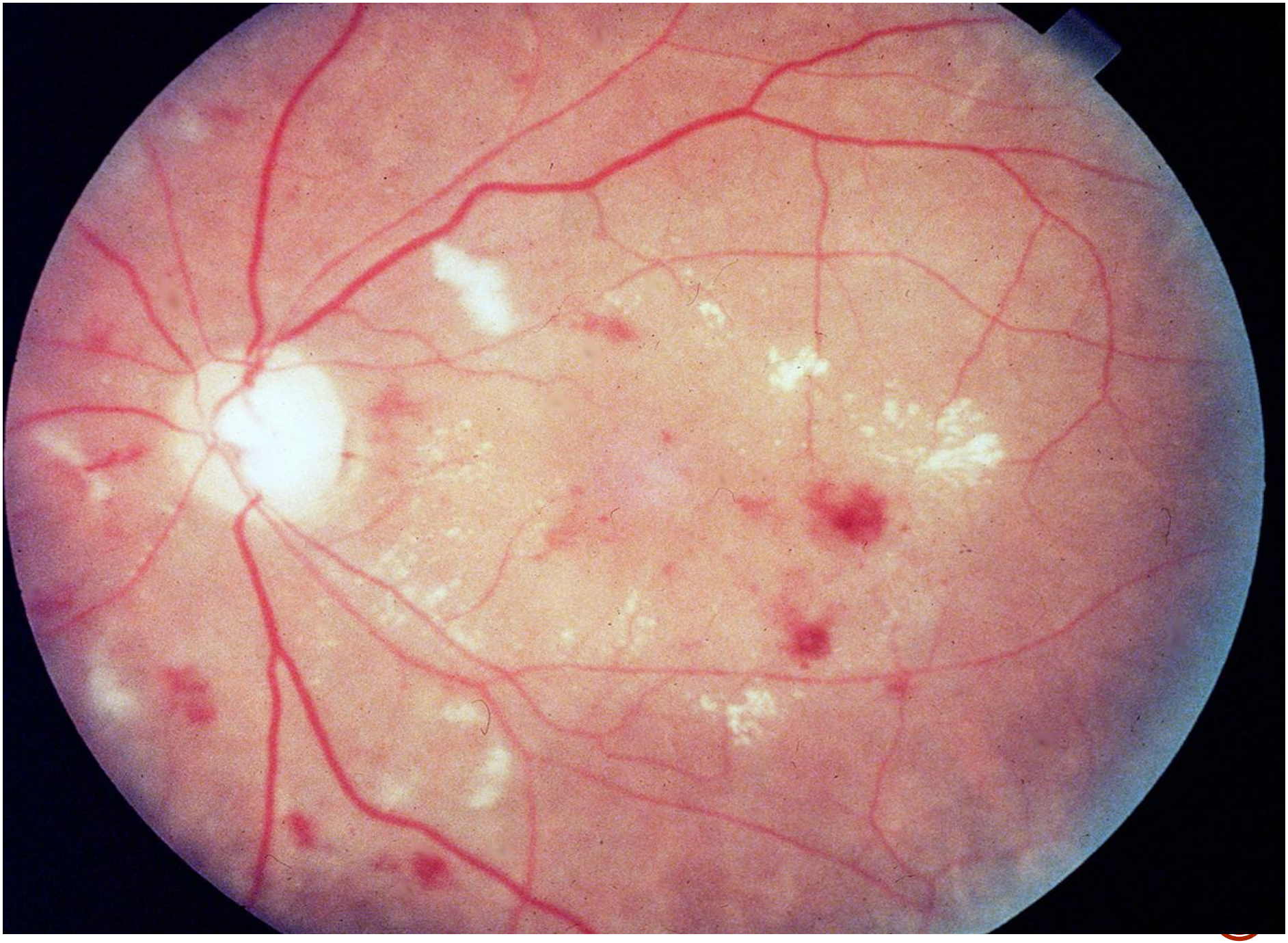
LONG TERM COMPLICATIONS OF DIABETES

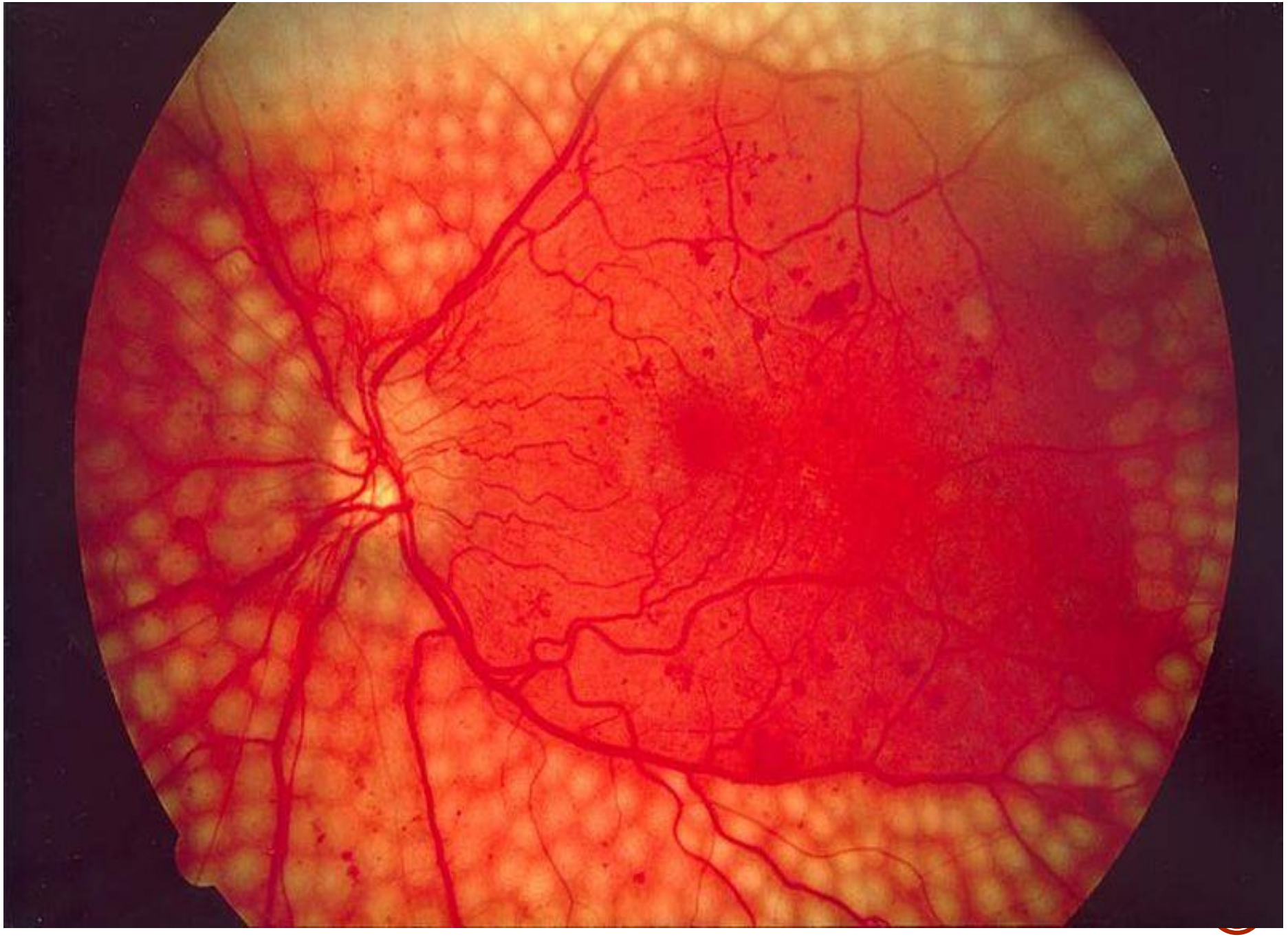
- Microvascular
  - Retinopathy
  - Nephropathy
  - Neuropathy *(autonomic vs. peripheral)*
- Macrovascular
  - Atheromatous disease

MANAGEMENT OF COMPLICATIONS

- ??







CASE 1

- 23 yr old man
- A&E -> Medics
- PC: weight loss, polyuria, polydipsia, vomiting and abdominal pain
- GP Ix:
  - dipstick urine: Glu 3+, Ketones 3+
  - BM: "Hi"

- *What's your differential dx?*

CASE 1

- *How would you manage this patient??*

- *What further investigations would you do??*

CASE 1

- Systems review: unremarkable
- PMHx: Nil
- FHx: Mother- DM. Dx age 62 "on tablets"
- DrugHx: Nil. NKDA.
- Social Hx: Chef in restaurant. Lives with family. Non-smoker. ETOH: nil. Denied illicit drug use

CASE 1

Examination:

- *General*:
  Unwell. Alert + orientated.
  Loose clothing++
  Dry mucous membranes++
  T 37.0 HR **120** BP **100/58** RR **26**

- *Cardio*: normal HS

- *Resp*: chest- vesicular BS

- *Abdo*: mild central abdo tenderness, no guarding/rebound

- *PNS + CNS*: unremarkable. Fundoscopy: normal

- *Feet*: no neurovascular compromise

CASE 1

- *Bloods*:

Na **125**	Hb 16	*VBG*:
K 4.0	MCV 90	pH **7.20**
Creat **120**	WCC **16**	pCO2 **2.4**
Urea **14**	Plts 349	pO2 6.5
		HCO3 **13**
Gluc **32**		B.E **- 8**
		Lact **2.0**

CASE 1

- *How would you treat this patient?*

CASE 1

- IV fluid resuscitation
- Fixed Rate Insulin Infusion;
  - 0.1 units/kg/hour
  - Maintain CBG > 14 with concurrent 10% dextrose until ketoacidosis resolves
- Monitor CBGs, VBGs, ketosis
- Inform HDU
- Diabetes Team review

CASE 1

- Insulin infusion discontinued- TDS novorapid + Glargine
- Diabetic Nurse education
- Dietician review

WHAT DO YOU NEED TO KNOW ABOUT DIABETES FOR FINALS?

- ~~Classification of diabetes~~
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- ~~Complications of diabetes~~
- ~~Diabetes emergencies~~

DIABETIC EMERGENCIES

- Diabetic Ketoacidosis
- Hyperosmolar Hyperglycaemia Syndrome
- Hypoglycaemia

HHS

- Diagnostic criteria?

HHS

- Diagnostic criteria?
  - Hyperglycaemia (CBG >30mmol/l)
  - Hyperosmolar (serum osmo > 340)
  - Ketones <+2

- Management?

HHS

- Diagnostic criteria?
  - Hyperglycaemia (CBG >30mmol/l)
  - Hyperosmolar (serum osmo > 340)
  - Ketones <+2

- Management?
  - Average fluid deficit 10-20L for 100kg man
  - Aim for ***slow***, consistent fall in osmolality
  - *??Insulin*

HYPOGLYCAEMIA

- CBG <4
- Conscious
  - What's the treatment?

HYPOGLYCAEMIA

- CBG <4

- Conscious
  - What's the treatment?

- Unconscious
  - What's the treatment?

BREAK TIME

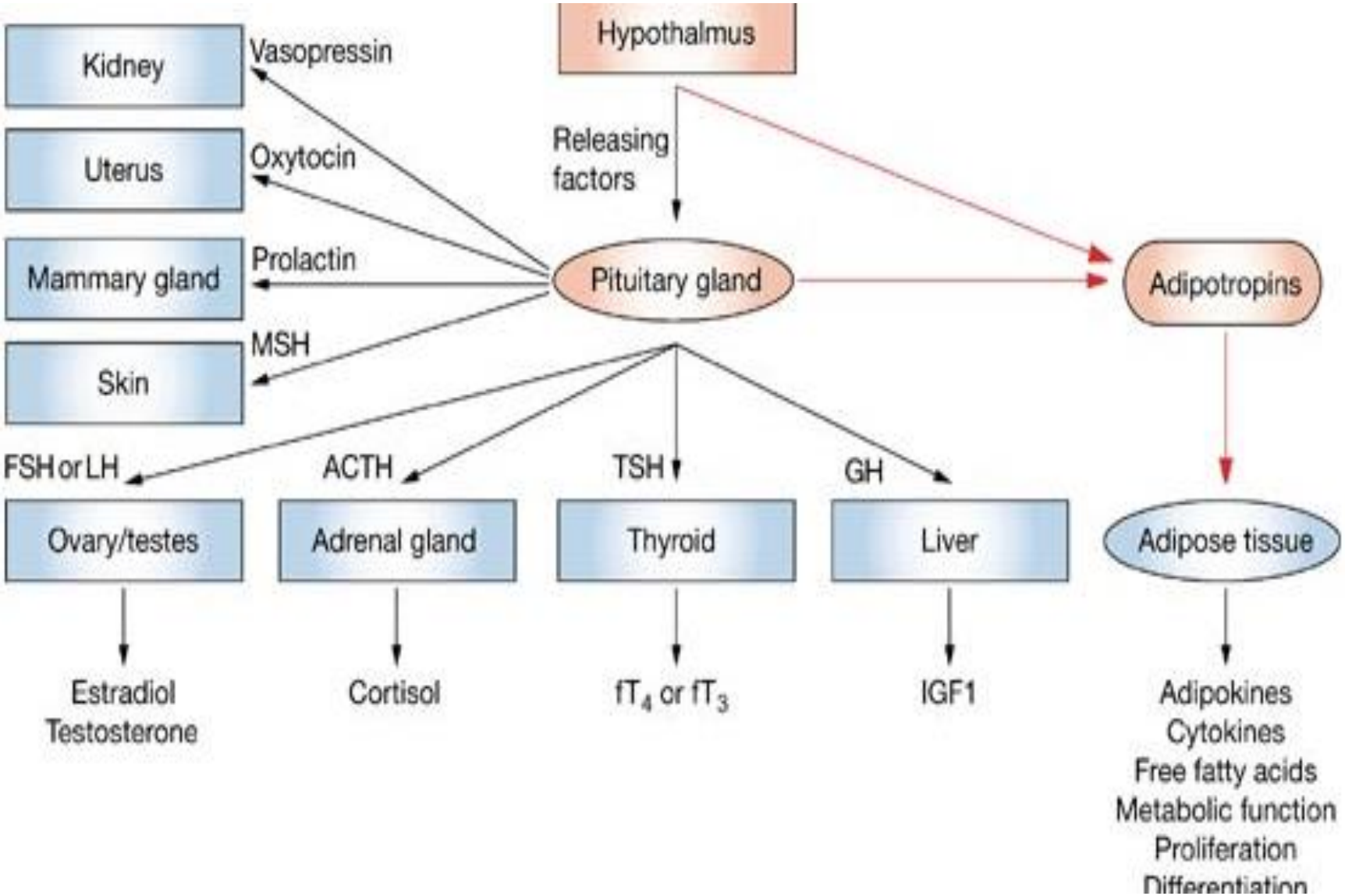
- STAND UP
- JUMP UP AND DOWN

BREAK TIME

- STAND UP
- JUMP UP AND DOWN
- ……OK, LET'S FINISH THIS TALK!

WHAT DO YOU NEED TO KNOW ABOUT ENDOCRINOLOGY FOR FINALS?

- Endocrine emergencies
- Pituitary disorders
- Thyroid disorders
- Parathyroid disorders
- Adrenal disorders


Hypothalmus
Releasing factors
Kidney
Vasopressin
Uterus
Oxytocin
Mammary gland
Prolactin
Skin
MSH
Pituitary gland
Adipotropins
FSH or LH
ACTH
TSH
GH
Ovary/testes
Adrenal gland
Thyroid
Liver
Adipose tissue
Estradiol
Testosterone
Cortisol
fT_4 or fT_3
IGF1
Adipokines
Cytokines
Free fatty acids
Metabolic function
Proliferation
Differentiation

WHAT DO YOU NEED TO KNOW ABOUT ENDOCRINOLOGY FOR FINALS?

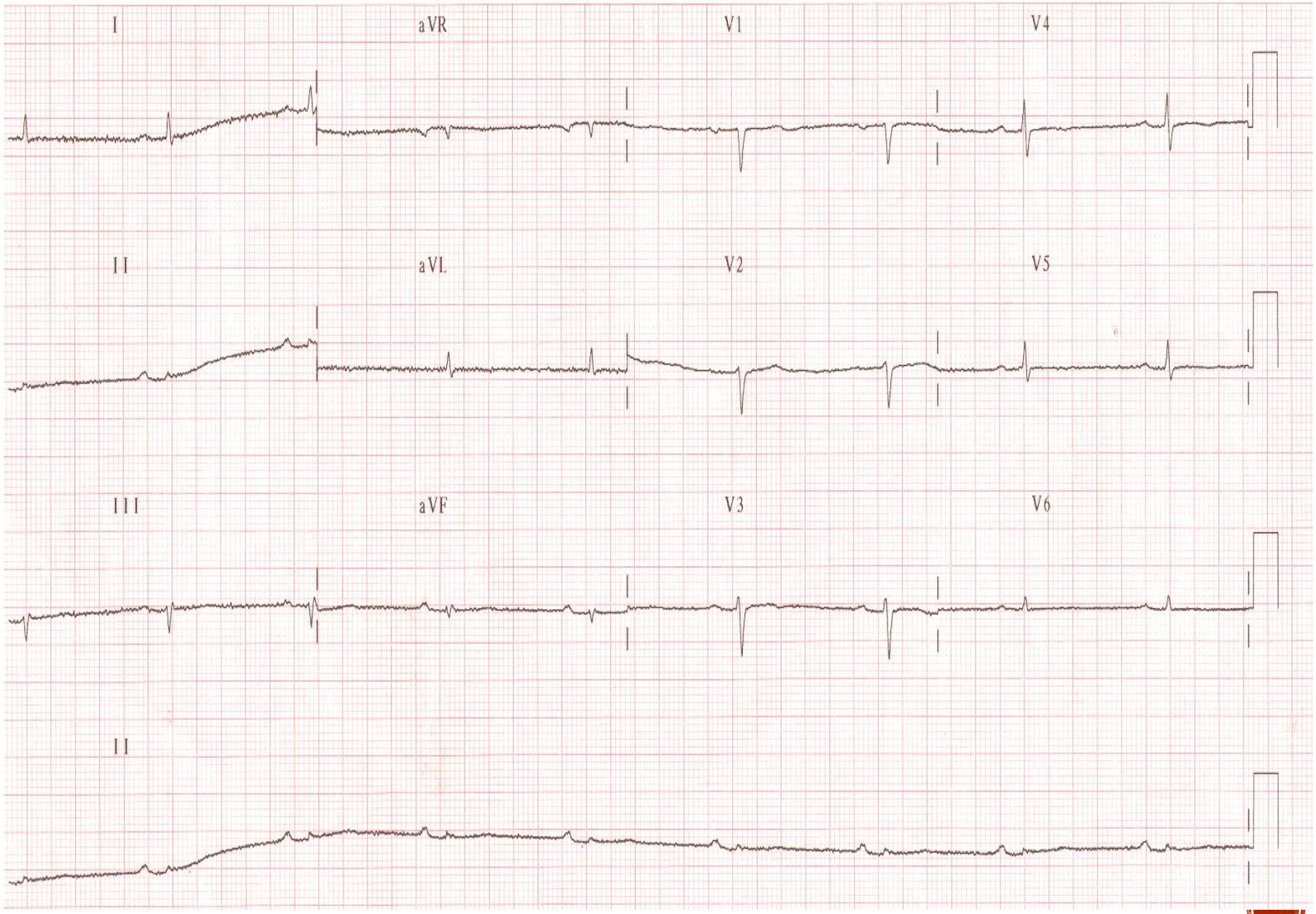
- Endocrine emergencies
- Pituitary disorders
- Thyroid disorders
- Parathyroid disorders
- Adrenal disorders

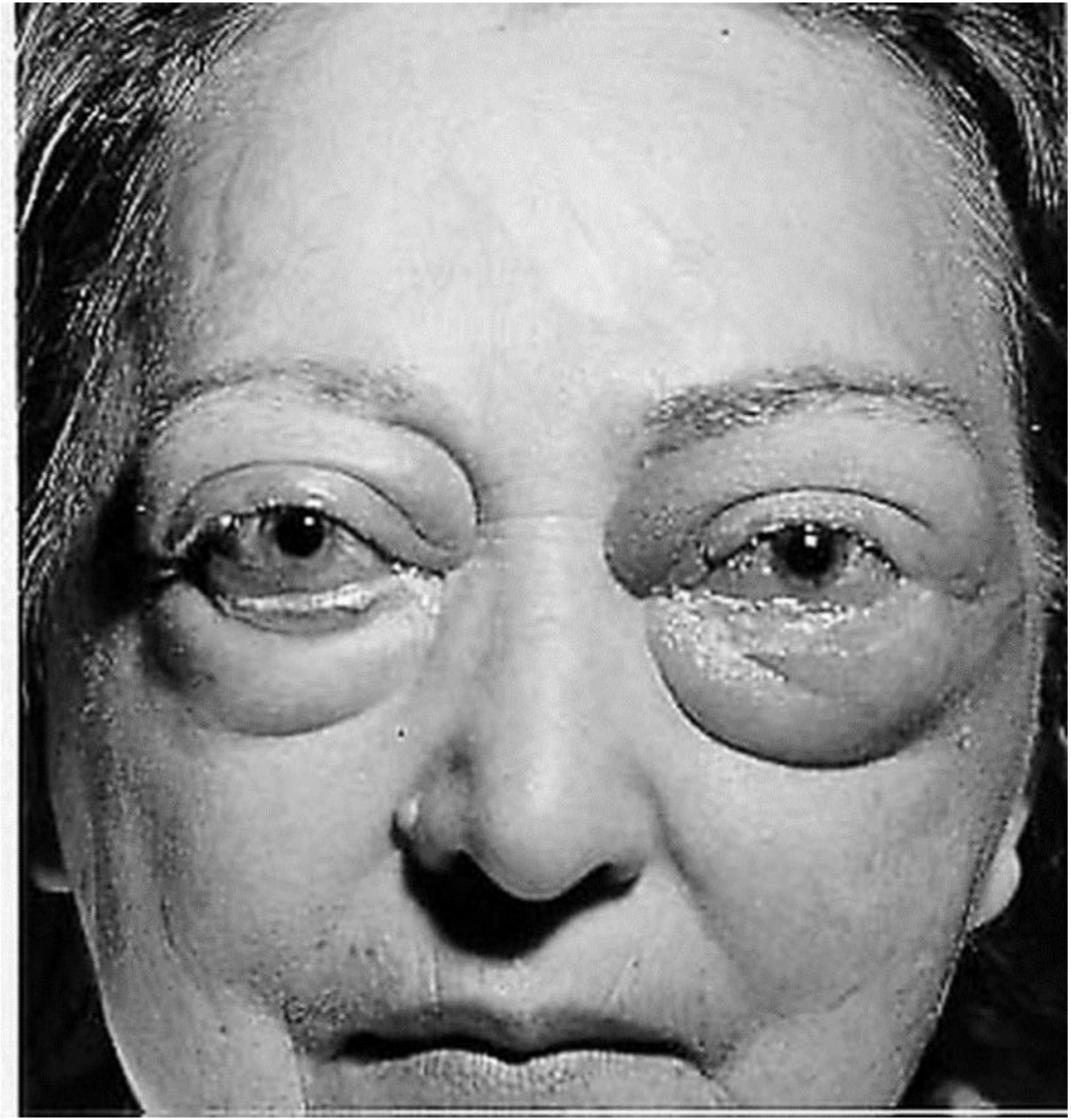
CASE 2

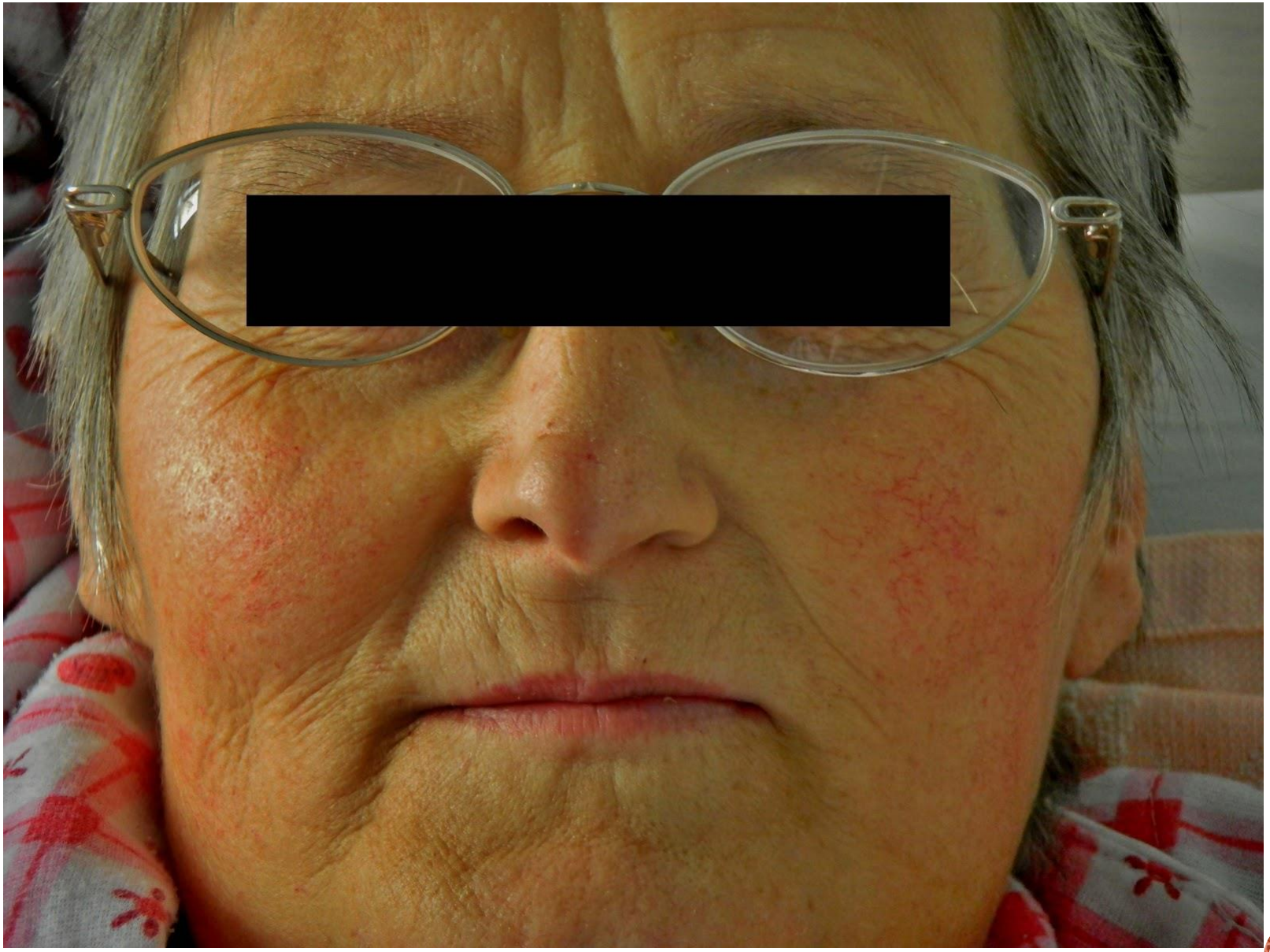
- 74 year old lady
- PC: confusion, reduced consciousness
- HPC: found by carer at home -> LAS.
- Increasing lethargy for past 2 months. "sleeping all the time". Reduced eating, drinking. "Puffy face"

CASE 2

- Observations;
  - Temperature 35.5
  - HR…….
  - BP 86/50
  - RR 10
  - Sats 98% RA


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II





CASE 2

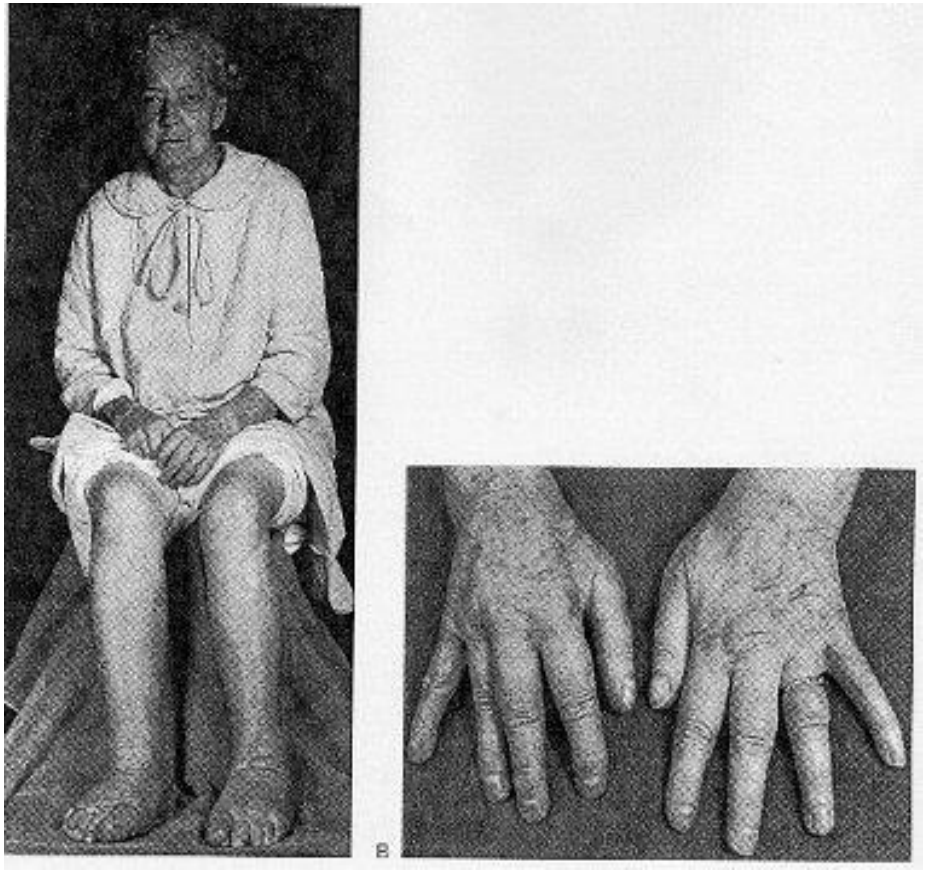
- What's the differential diagnosis?
- How would you manage this patient?
- How would you treat this patient?

MYXEDEMA COMA

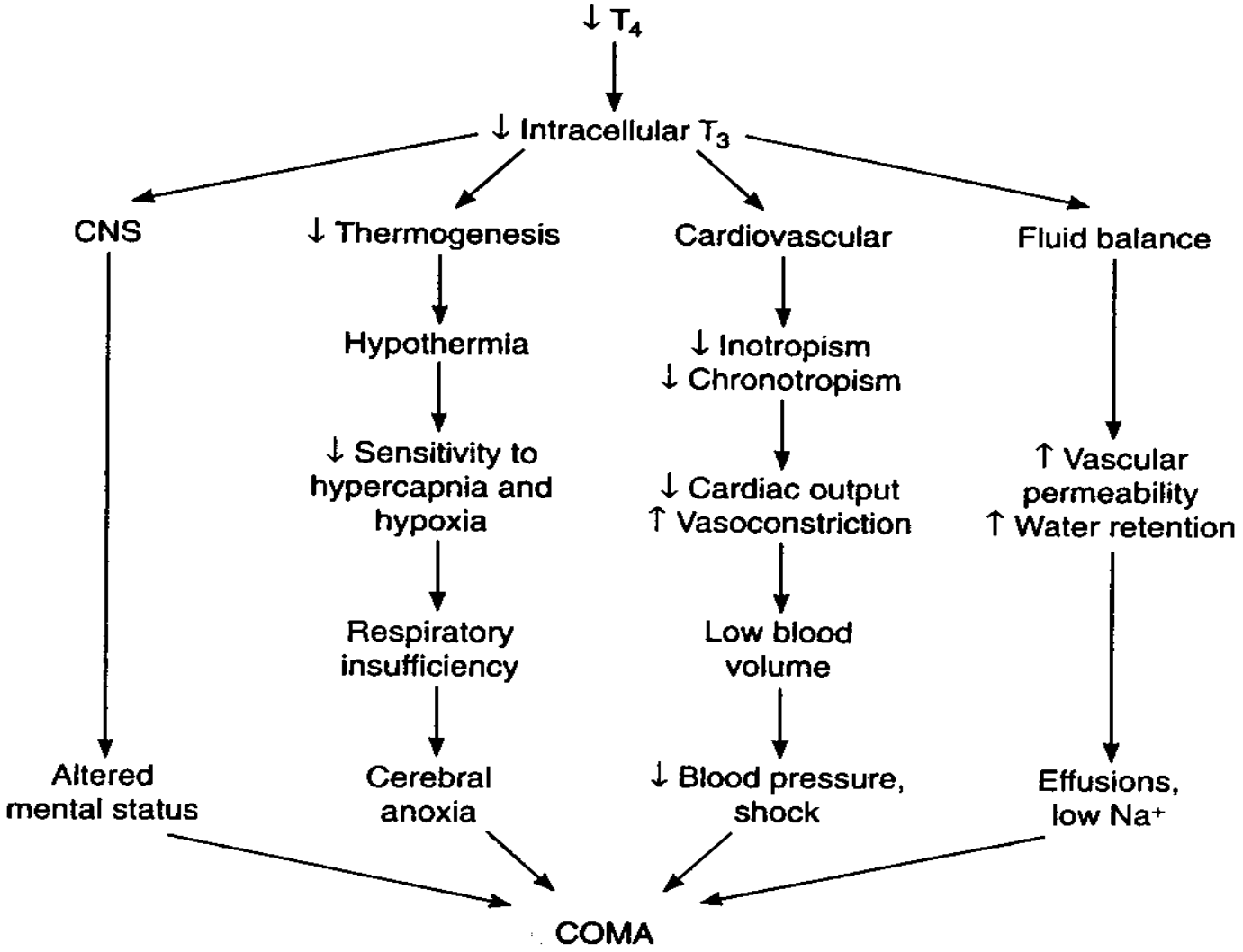
- End stage of untreated or insufficiently treated hypothyroidism
- Typical clinical picture:
  - Elderly obese female
  - Becoming increasingly withdrawn, lethargic, sleepy and confused
  - coma
- History:
  - Previous thyroid surgery
  - Radioiodine
  - Default thyroid hormone therapy
- **MORTALITY IS 20%**

PHYSICAL FINDINGS

- Comatose or semi comatose
- Dry coarse skin
- Hoarse voice
- Thin dry hair
- Delayed reflex relaxation time
- Hypothermia
- Pericardial, pleural effusions, ascites



PATHOGENESIS OF MYXEDEMA



LAB TESTS

- Free **T4 low** and **TSH high**
- If the T4 is low and TSH low normal consider ??

- Distinguish from sick euthyroid syndrome
  - Low T3, Normal or low TSH, normal free T4

MANAGEMENT OF MYXEDEMA (1)

- ICU admission may be required for ventilatory support and IV medications
- Parenteral thyroxine
  - Loading dose of 300 – 400 μg
  - Then 50 μg daily

MANAGEMENT OF MYXEDEMA (2)

- Electrolytes
  - Water restriction for hyponatremia
  - Avoid fluid overload
- Avoid sedation
- Glucocorticoids
  - Controversial but necessary in hypopituitarism or multiple endocrine failure
  - Dose: Hydrocortisone 40 – 100 mg 6 hly for 1 week, then taper

CASE 3

- 44 yr old

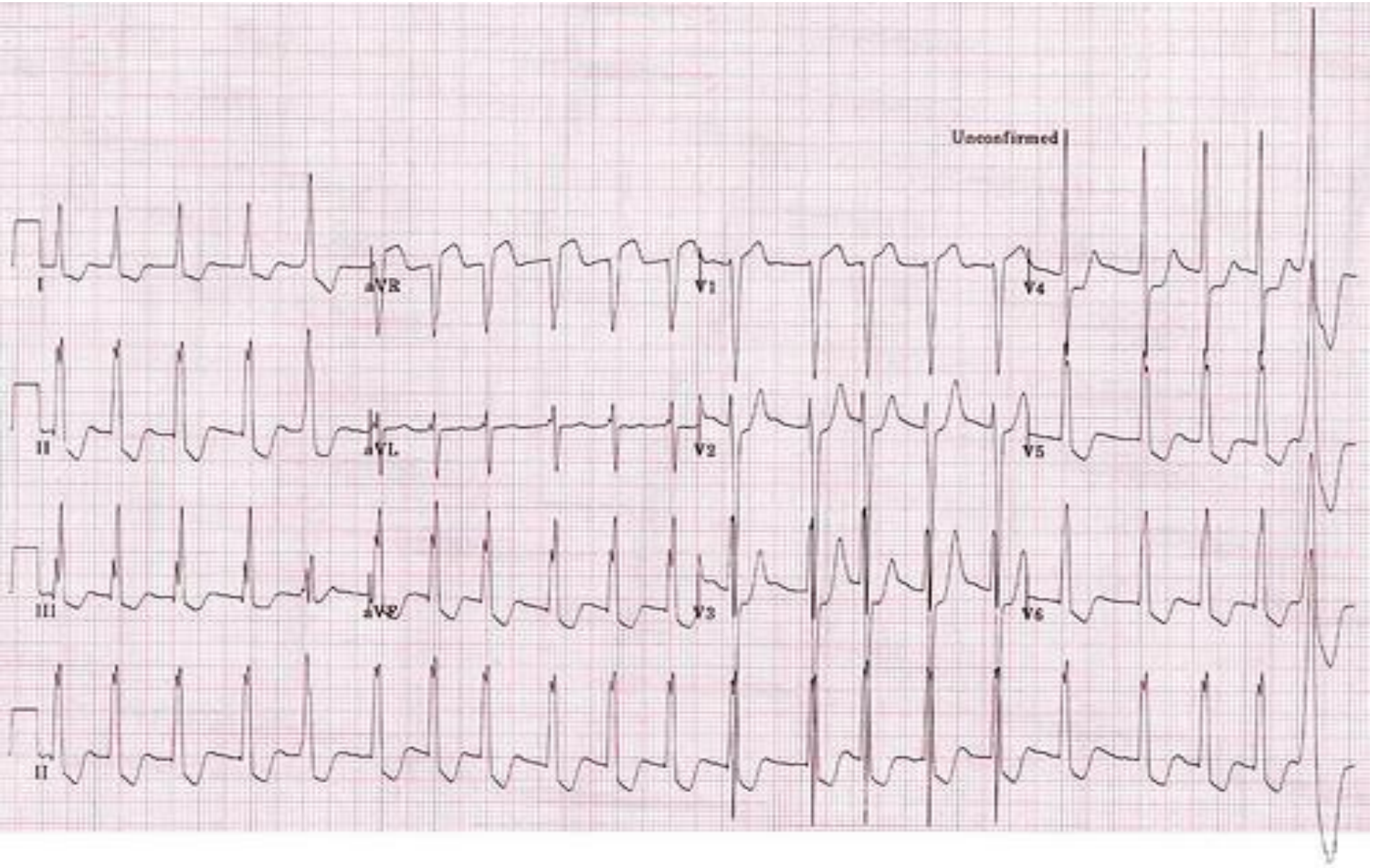
- PC: ?Psychotic symptoms -> referred to Psych

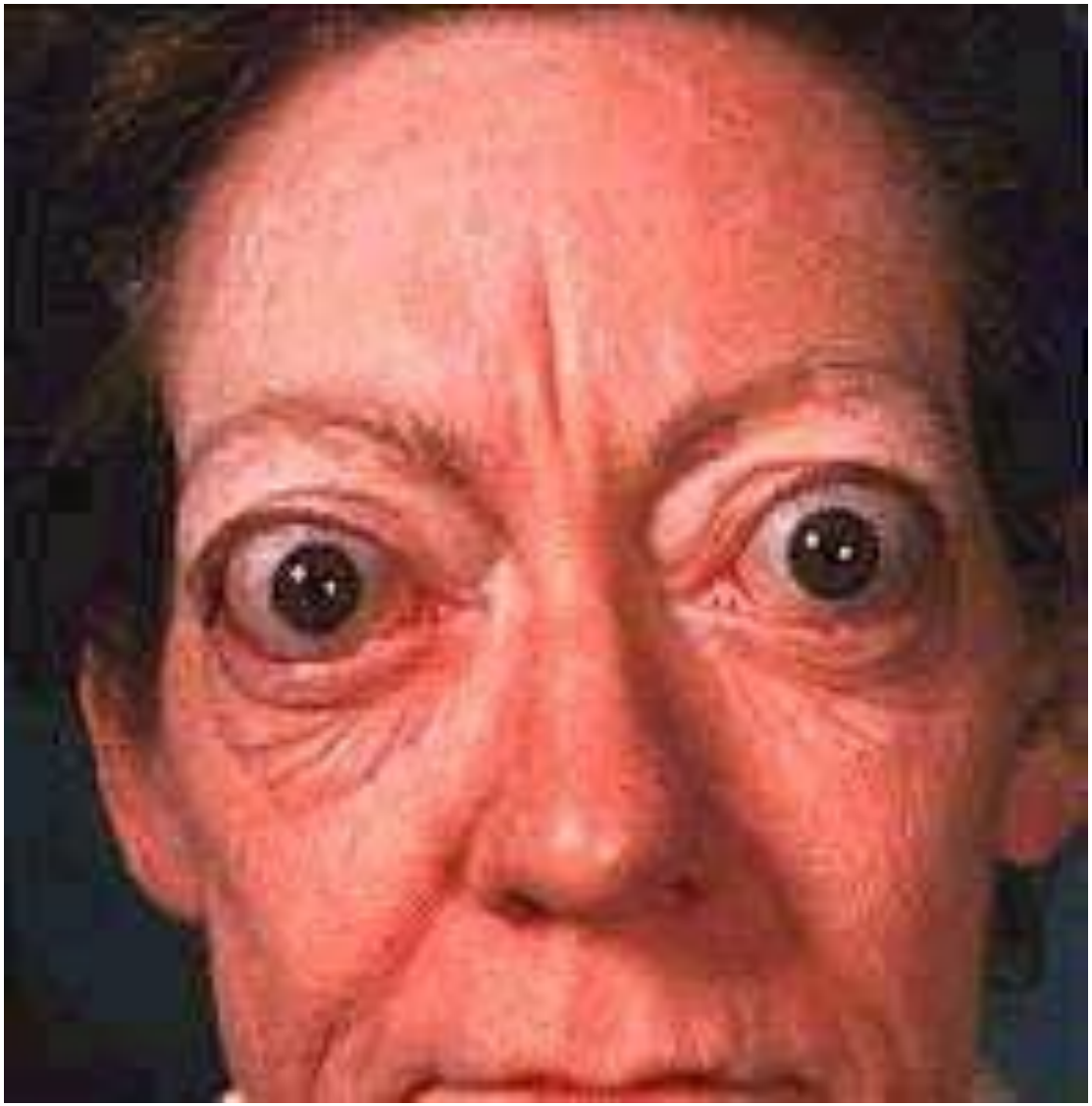
  They requesting a "Medical opinion"

- HPC: Weight loss, worsening "manic type symptoms", poor concentration

CASE 3

- Observations;
  - Temp 39.0
  - HR 140
  - BP 155/87
  - RR 30
  - Sats 98% RA


Unconfirmed
I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II



CASE 3

- What's the differential diagnosis?
- How would you manage this patient?
- How would you treat this patient?

THYROID STORM

Acute life threatening exacerbation of thyrotoxicosis

CLINICAL SETTING

- Patient with Graves disease who has discontinued antithyroid medication OR previously undiagnosed
- Hyperpyrexia (>40 ^{0}C)
- Sweating
- Tachycardia with or without AF
- Nausea, vomiting and diarrhea
- Tremulousness and delirium, occasionally apathetic

PRECIPITATING FACTORS

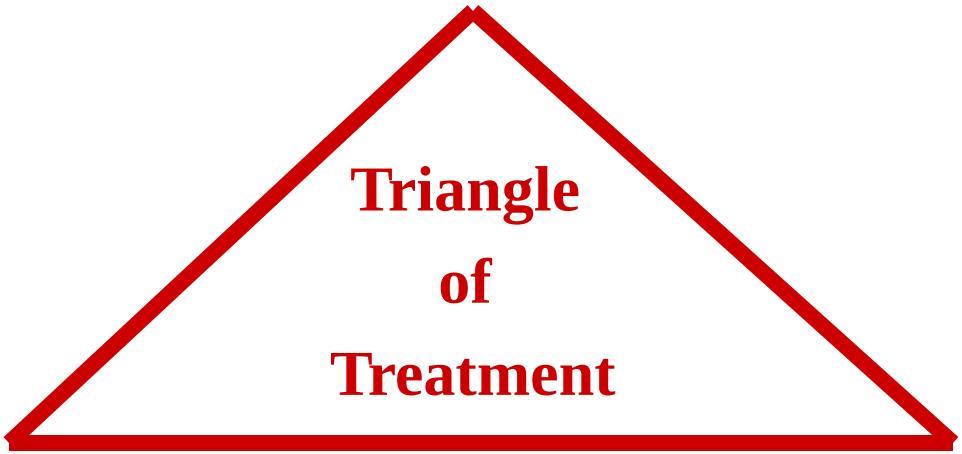
- Withdraw of antithyroid drugs
- Severe infection
- DKA
- CVI
- Cardiac failure
- Surgery
- Trauma
- Radioiodine
- Drug reaction
- Iodinated contrast medium

DIAGNOSIS

- **Free T4, free T3 elevated**
- **TSH suppressed**
- **In Graves' Thyroid Perioxidase Antibodies strongly positive**
- **US thyroid**
- **NM Thyroid (once stable)**

TREATMENT OF THYROID STORM

⇓ **Sympathetic outflow**



⇓**Production and release of thyroid hormone**

⇓**Peripheral conversion (T4 → T3)**

MANAGEMENT OF THYROID STORM (1)

- Supportive care
  - Fluids, containing Glucose
  - Oxygen
  - Cooling
  - If indicated antibiotics or digoxin

MANAGEMENT OF THYROID STORM (2)

- Specific Measures
  - Propranolol PO or iv infusion
  - Propylthiouracil (NG/PO or PR)
  - Lugol's Iodine or Potassium Iodide PO
  - Hydrocortisone 6 hly

PROGNOSIS

- Mortality dropped since the 1920's from 100% to 20 – 30%
- Mortality most frequently associated with serious underlying medical conditions

CAUSES OF THYROTOXICOSIS

- ??

CASE 4

- 25 yr old
- PC: Collapse.
- HPC: Recent dx UTI -> PO Abx by GP

  Vomiting, abdo pain

  Lethargy

  Weight loss 5 kg in 1/12

CASE 4

- Observations;
  - Temp 37.9
  - HR 110
  - BP 80/45
  - RR 28
  - Sats 98% RA
  - BM 2.8

CASE 4

- What's the differential diagnosis?
- How would you manage this patient?
- How would you treat this patient?

ACUTE ADRENAL INSUFFICIENCY

CAUSES OF ACUTE ADRENAL INSUFFICIENCY (1)

- Usually presents as an acute process in a patient with underlying chronic adrenal insufficiency

- Causes of Primary adrenal insufficiency
  - Auto-immune
  - TB
  - Metastatic malignancy to adrenals
  - HIV related infections

CAUSES OF ACUTE ADRENAL INSUFFICIENCY (2)

- Causes of secondary adrenal insufficiency
  - Pituitary or hypothalamic disease

- Acute destruction of the adrenals can occur with bleeding in the adrenals
  - Sepsis
  - DIC or
  - complication of anticoagulant therapy

PRECIPITATING EVENTS (1)

- Omission of medication
- Precipitating illness
  - Severe infection
  - Myocardial infarction
  - CVI
  - Surgery without adrenal support
  - Severe trauma

- Withdrawal of steroid therapy in a patient on long term steroid therapy (adrenal atrophy) ***Iatrogenic Adrenal Insufficiency***

PRECIPITATING EVENTS (2)

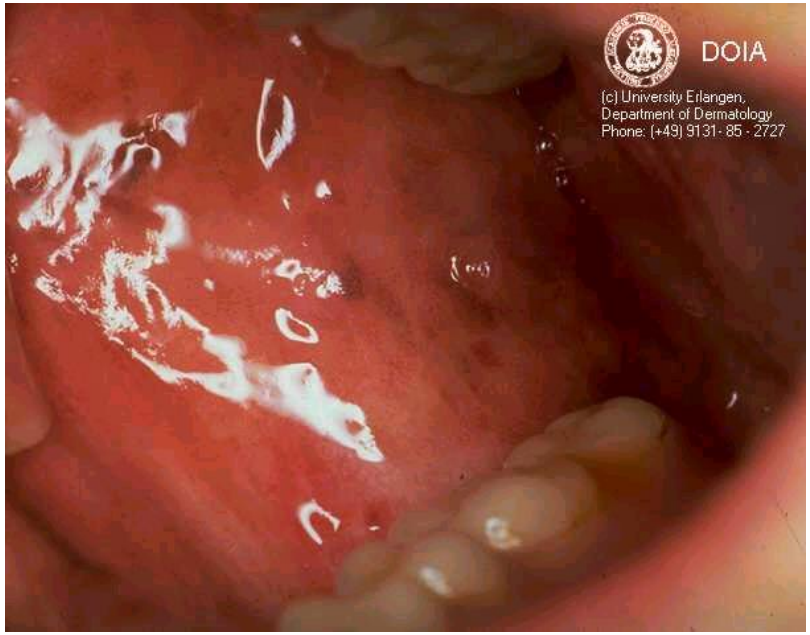
- Administration of drugs impairing adrenal hormone synthesis e.g. Ketoconazole
- Using drugs that increase steroid metabolism e.g. Phenytoin and rifampicin

CLINICAL PRESENTATION

- Nausea and vomiting
- Hyperpyrexia
- Abdominal pain
- Dehydration
- Hypotension and shock

CLUES TO UNDERLYING PRIMARY ADRENAL INSUFFICIENCY

- Pigmentation in unexposed areas of the skin
  - Creases of hands
  - Buccal mucosa
  - Scars
- Consider adrenal insufficiency if hypotension does not respond to pressors



LAB DIAGNOSIS (1)

- **Hyponatremia and hyperkalemia** (Hyponatremia might be obscured by dehydration)
- Random cortisol is not helpful unless it is very low (<5 mg/L) during a period of great stress

- 9am cortisol

- What are normal cortisol dynamics??

LAB DIAGNOSIS (2)

- ACTH (syn**acth**en) stimulation test
  - Failure of cortisol to rise above 580 nmol/L 30 min after administration of 0.25 mg of synthetic ACTH sc

- Basal ACTH will be raised in primary adrenal insufficiency but not in secondary

- CT of abdomen will reveal enlargement of adrenals in patents with adrenal hemorrhage, active TB or metastatic malignancy

MANAGEMENT OF ACUTE ADRENAL INSUFFICIENCY (1)

- Hydrocortisone
  - 100 mg IM stat then 50-100 mg 4 hly for 24 h
  - Taper slowly over the next 72 h
  - change to oral replacement therapy once E&D
  - Overlap the first oral and last IM doses

- Replace salt and fluid losses IV fluids

MANAGEMENT OF ACUTE ADRENAL INSUFFICIENCY (2)

- Patients with primary adrenal insufficiency may require mineralocorticoid therapy (fludrocortisone) when shifted to oral therapy

- Monitor postural hypotension, electrolytes

PITUITARY DISORDERS

- Pituitary tumours
  - Local Compression
    - Failure of normal pituitary function
    - Bitemporal hemianopia
    - III, IV and VI palsy
    - Loss of dopaminergic control and hyperprolactinaemia
  - Uncontrolled hormone release
    - ACTH – Cushing's Disease
    - GH – Acromegaly
    - LH / FSH – typically NFPA
    - Prolactin
    - TSH – (rare)

PITUITARY APOPLEXY

CLINICAL SETTING

- Sudden crisis in a patient with known or previously unknown pituitary tumor

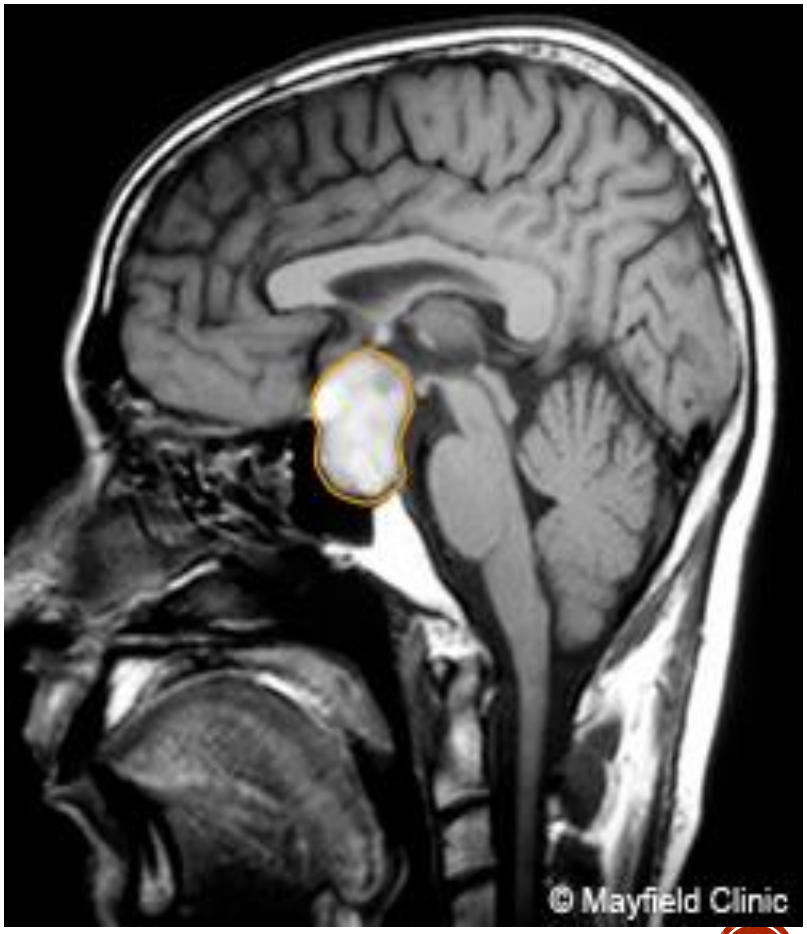
- It may occur in a normal gland during and after child birth, or with head trauma, or in patient on anticoagulation therapy

SYMPTOMS AND SIGNS

- Severe headache and visual disturbance
- Bitemporal hemianopia
- N III palsy
- Meningeal symptoms with neck stiffness
- Symptoms of acute secondary adrenal insufficiency
  - Nausea vomiting , hypotension and collapse

DIAGNOSIS

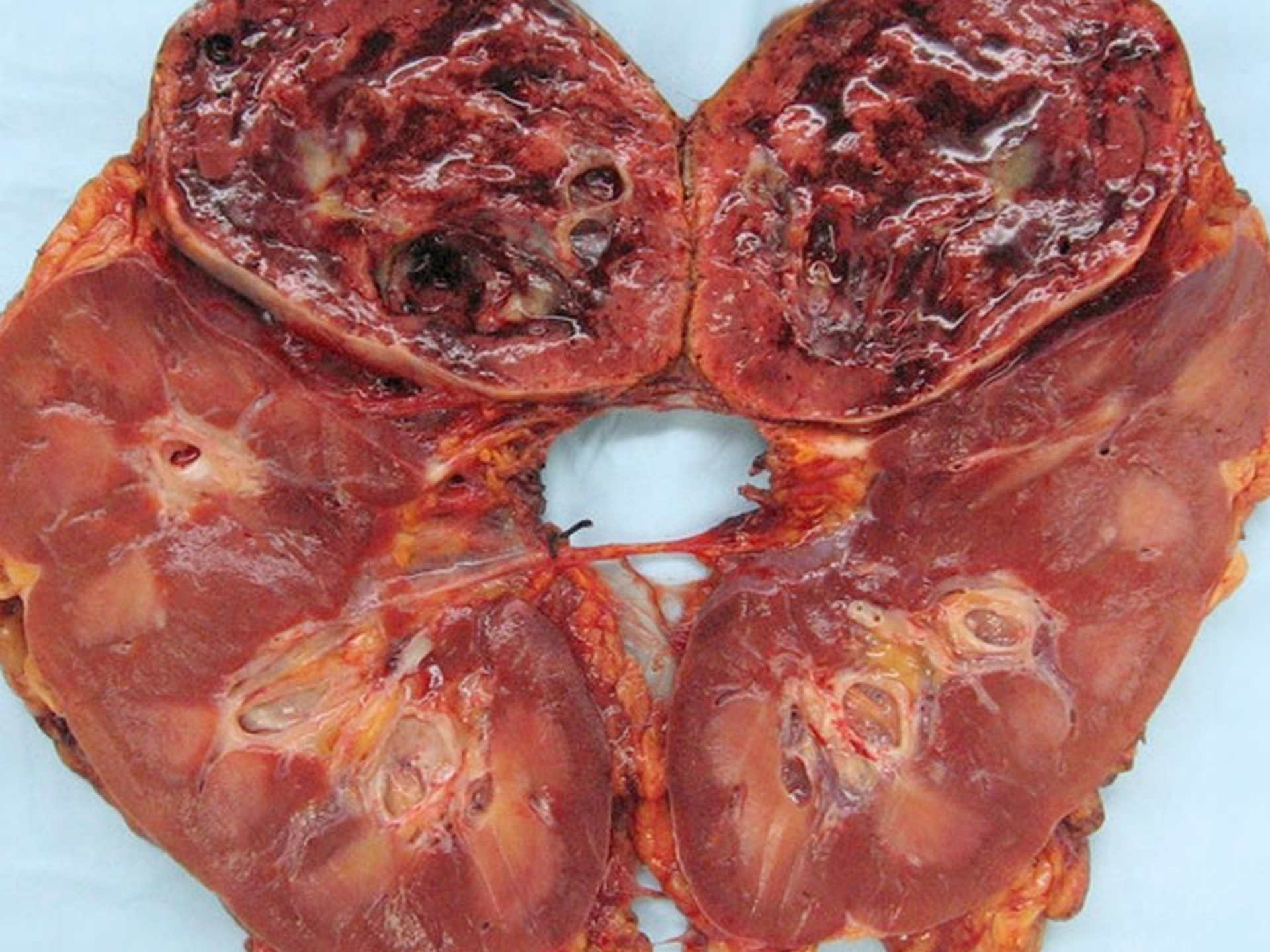
- CT scan of head and pituitary
- Hormonal studies only of academic interest
- Assessment of pituitary function after acute stage has settled



MANAGEMENT OF PITUITARY APOPLEXIA

- Hormonal
  - Hydrocortisone (glucocorticoid support and relief of ?cerebral edema)
- ?Neurosurgical intervention
  - Transsphenoidal pituitary decompression

After the acute episode the patient must be evaluated for multiple pituitary deficiencies



PHEOCHROMOCYTOMA CRISIS

CAUSES

- Action of unopposed high circulating levels of catecholamines
  - α - receptors: Pressor response
  - β - receptors: positive ino- and chronotopic
- Precipitating factors
  - Spontaneous
  - Haemorrhage into pheochromocytoma
  - Exercise
  - Pressure on abdomen
  - Urination
  - Drugs: glucagon, naloxone, metoclopramide, ACTH, cytotoxics, TAD

CLINICAL FEATURES

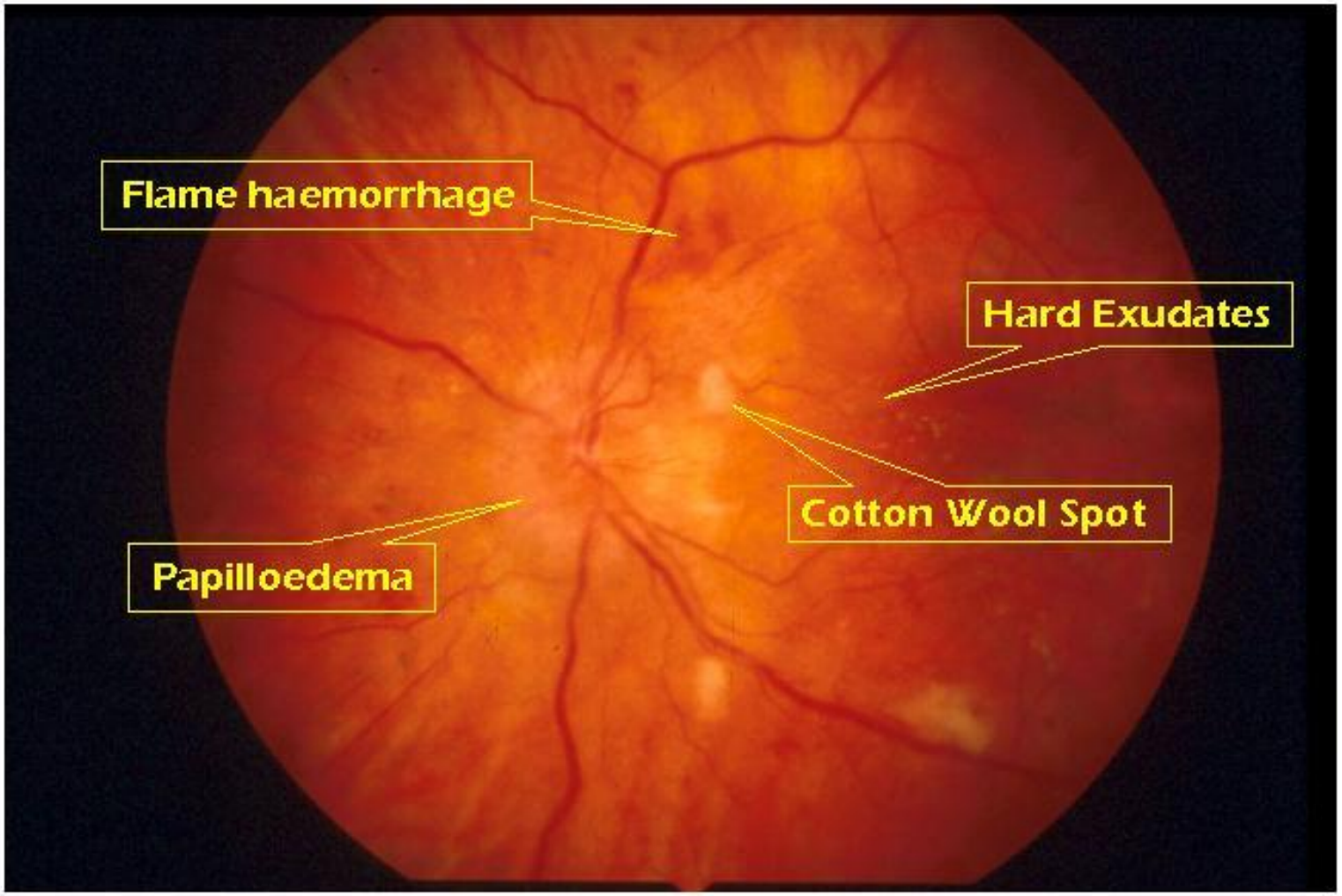
- History of poorly controlled Hypertension or accelerated Hypertension

- **Hypertension, palpitations, sweating**, pallor, pounding headache, **anxiety**,tremulousness, pulmonary edema, **feeling of impending death**, hyperhydrosis, nausea and vomiting, abdominal pain, paralytic ileus hyperglycaemia, hypertensive encephalopathy, myocardial infarction and stroke

CLINICAL FETAURES

- Attacks build up over a few minutes and fade gradually over 15 min or can be more sustained (60 min)
- Signs of end organ damage

Hypertensive Retinopathy - Grade 4



BIOCHEMICAL DIAGNOSIS

- 24h urine collection for free catecholamines and metanephrines

TREATMENT

- Do not wait for biochemical confirmation of the diagnosis
- α - antagonists: Phenoxybenzamine, Doxazosin
- Non selective β- antagonist: Propranolol
- Treatment with α - antagonists should precede β- antagonist treatment with 48 h to avoid exacerbation of the crisis
- Be aware of postural hypotension

ACUTE HYPERCALCAEMIA

MOST COMMON CAUSES

- Endocrine:
  - Hyperparathyroidism
  - MEN
  - PTHrp by solid tumors
- Neoplastic:
  - Ca with bone metastases
  - Myeloma
- Granulomatous:
  - Sarcoidosis
  - Tuberculosis

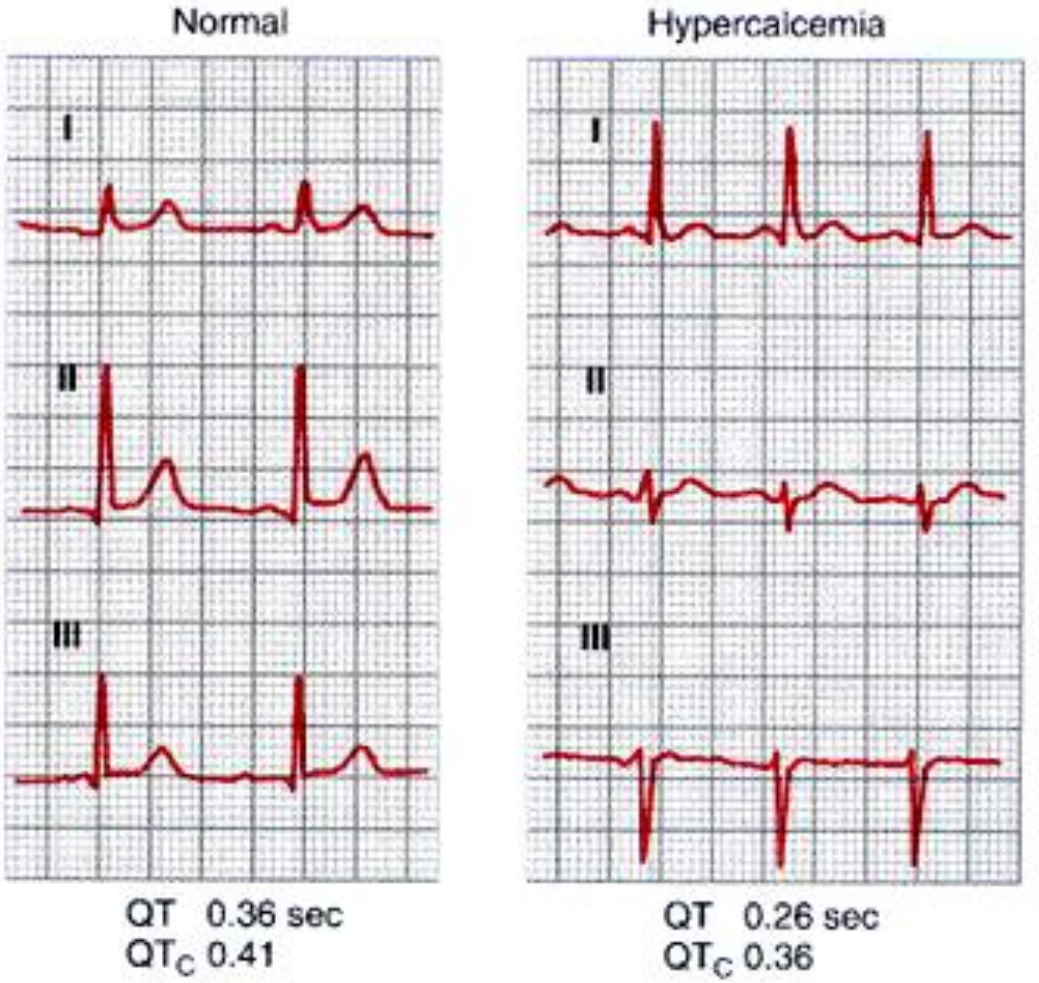
- **What's the commonest cause??**

CLINICAL FEATURES

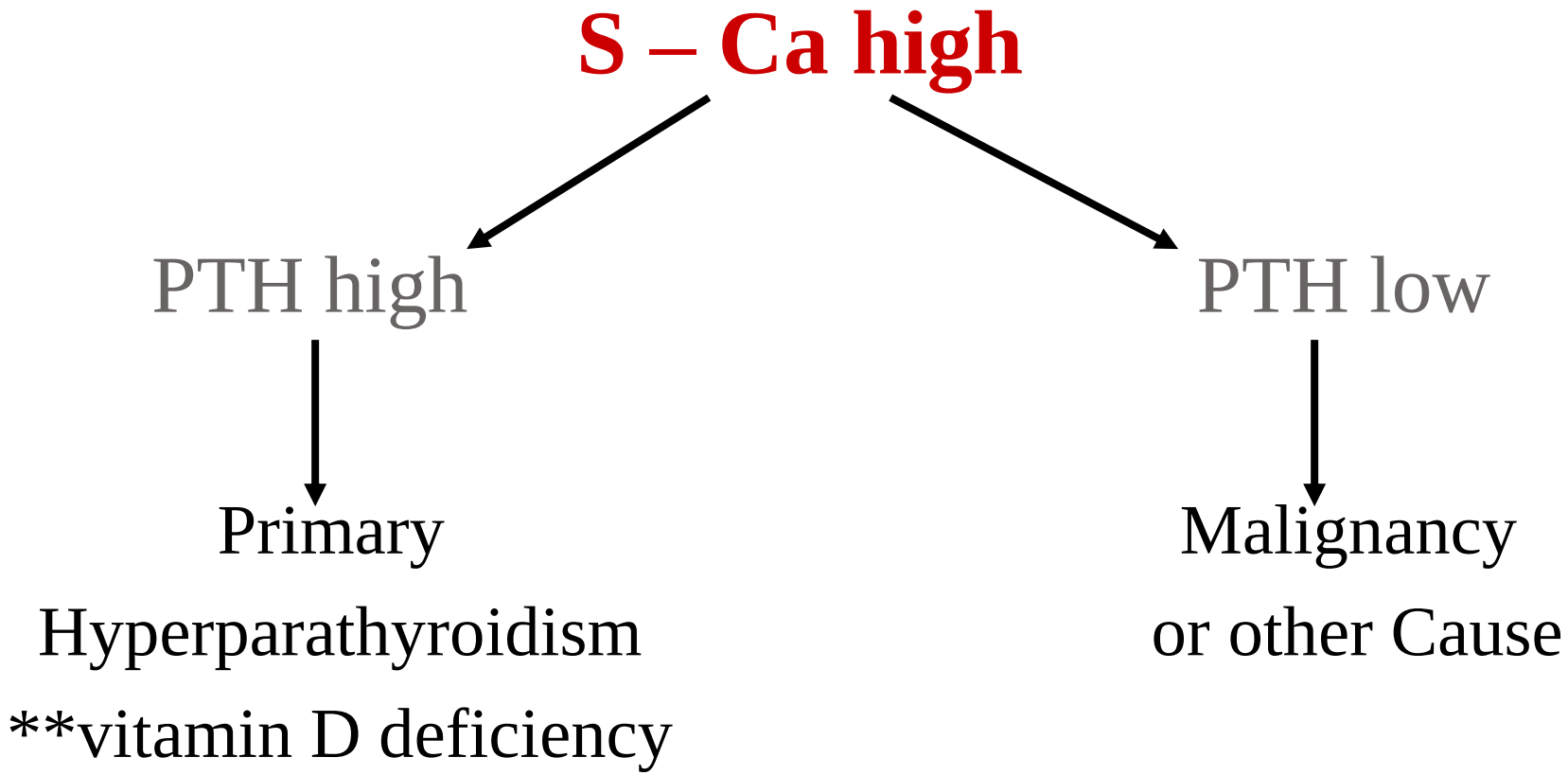
- History of polyuria and polydipsia
- Dehydration
- Bone pain
- Confusion
- Anorexia
- Constipation

- " BONES, STONES, GROANS AND ABDOMINAL MOANS"

ECG HYPERCALCEMIA



WORKUP



S – Ca > 3.0 is 90% of the time of malignant origin

TREATMENT OF HYPERCALCAEMIA

- Volume repletion and diureses
  - NaCl 0.9% 4 L in first 24 h
  - Loop diuretics (furosemide has calciuretic effects)
- Bisphosphonates IV (Pamidronate)
- Corticosteroids (prednisone 30 – 60 mg daily) are the drugs of choice if granulomatous disease or vit A or D intoxication is the cause

ACUTE HYPOCALCAEMIA

CAUSES OF ACUTE HYPOCALCAEMIA (1)

- Hypoparathyroidism
  - Destruction of parathyroids
    - Most commonly surgical – parathyroid resection or accidental
  - Acute hypomagnesaemia
- Reduced 1,25(OH)vit D
  - Chronic renal insufficiency
  - Acute systemic illness
  - Drugs: ketoconazole, doxorubicin, cytarabine

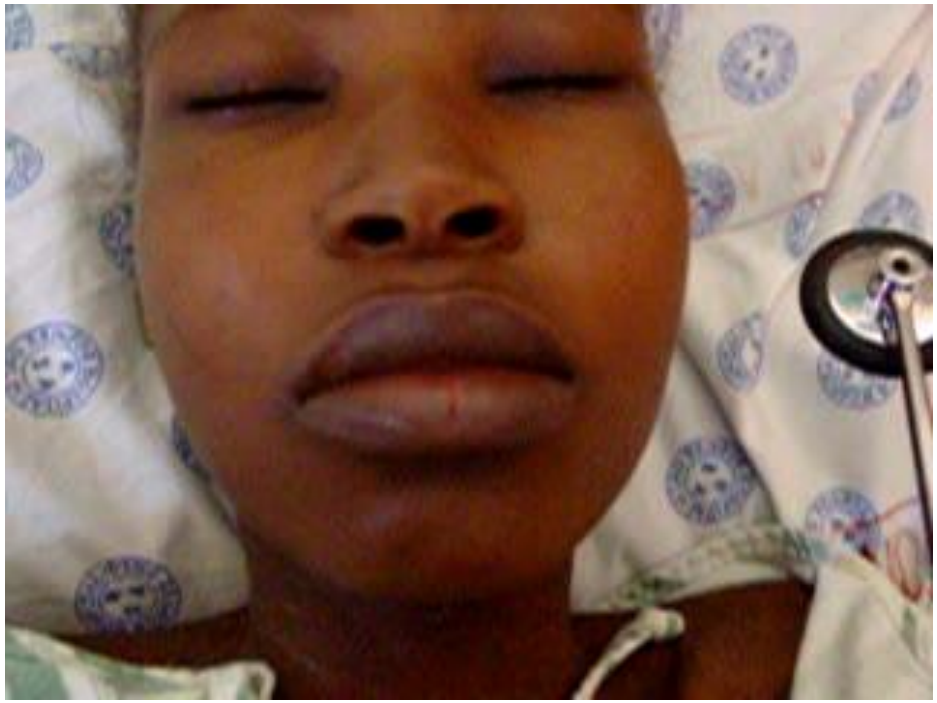
CAUSES OF ACUTE HYPOCALCAEMIA (2)

- Increased uptake of Ca in bone
  - Osteoblastic metastases
  - Hungry bone syndrome
- Complexing of Ca from the circulation
  - ↑ albumin binding in alkalosis
  - Acute pancreatitis with formation of Ca soaps
  - Transfusion related citrate complexing

CLINICAL PICTURE OF ACUTE HYPOCALCAEMIA

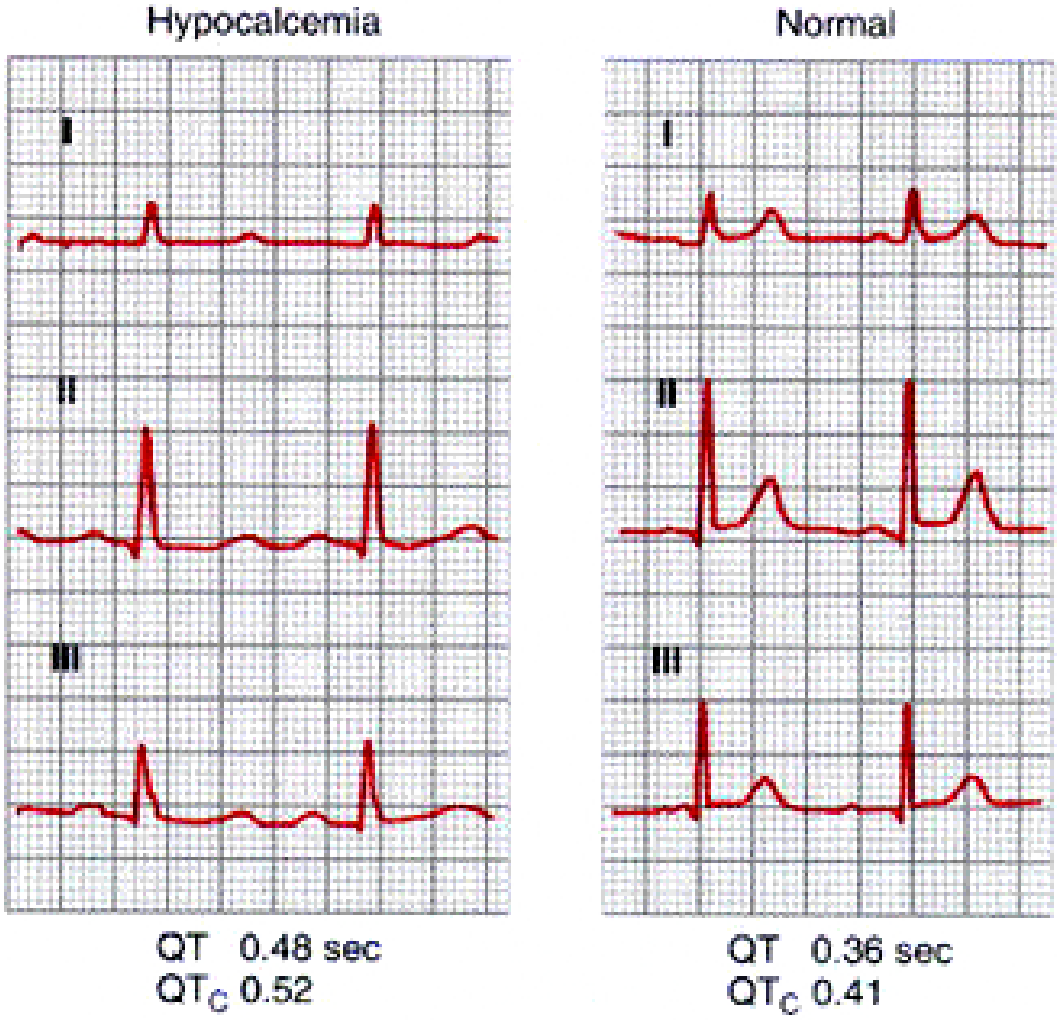
- Symptoms
  - Perioral numbness
  - Tingling parasthesias
  - Muscle cramps
  - Carpopedal spasm
  - Seisures
- Signs
  - Hyperreflexia
  - Chvostek sign
  - Trousseau sign
  - Hypotension
  - Bradicardia
  - Prolonged QT interval
  - Arrhythmias

CHVOSTEK SIGN



TROUSSEAU SIGN

ECG IN HYPER AND HYPOCALCEMIA !!

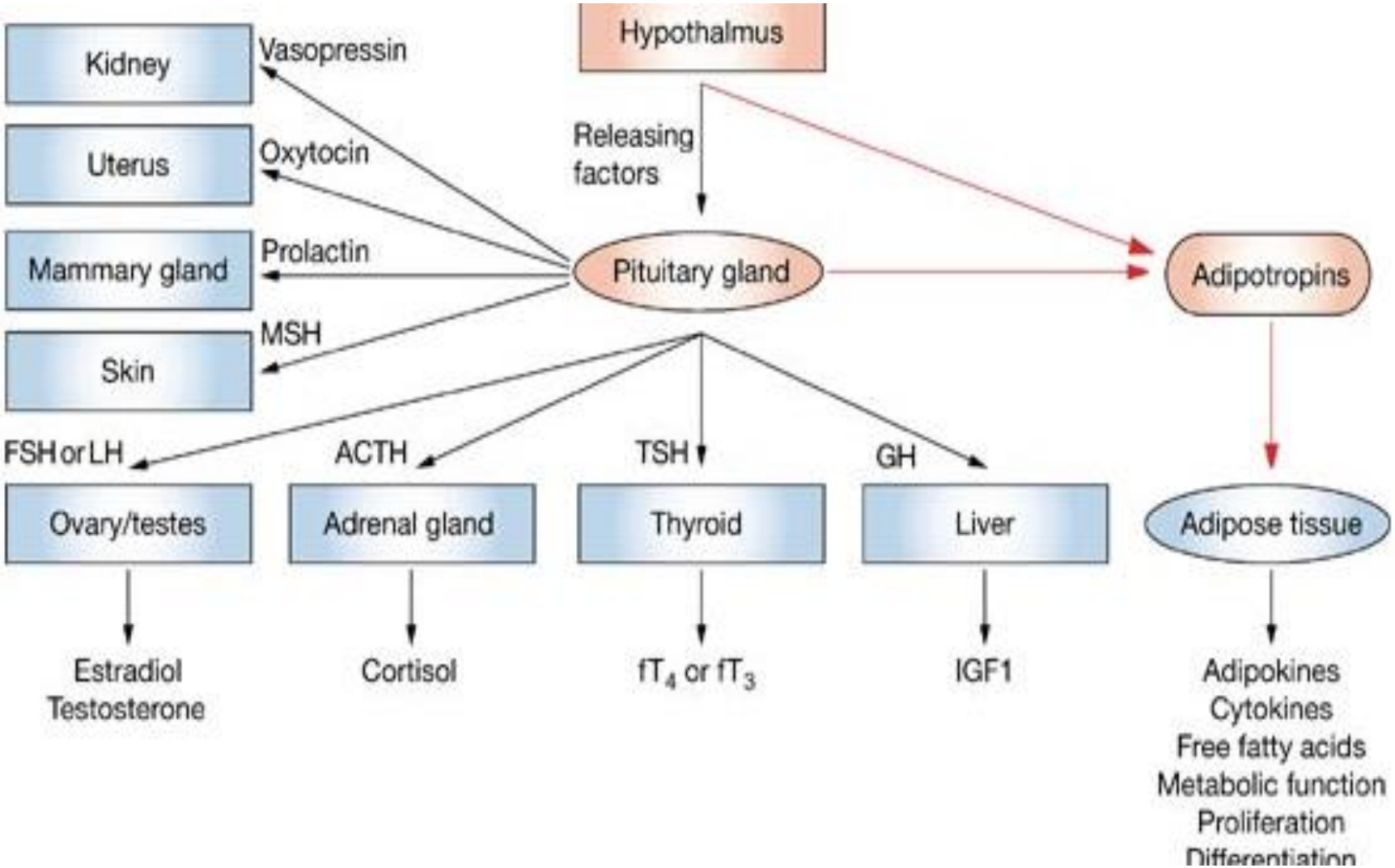


BIOCHEMICAL WORKUP

- total Ca^{++}, Albumin and Ionized Ca^{++}
- PO_4^{++}
- Mg^{++}
- Plasma PTH
  - Low in hypoparathyroidism
  - High in hungry bones syndrome /tertiary hyperparathyroidism
- $25(OH)D_3$ and $1,25\ (OH)D_3$

TREATMENT OF HYPOCALCEMIA

- First correct low Mg^{++}
- Calcium gluconate 10 ml of 10% solution IV over 5 – 10 min and repeat as necessary in cases with frank generalized tetany
- Slower continuous infusion of Calcium gluconate in less acute cases


Hypothalmus
Releasing factors
Pituitary gland
Kidney
Vasopressin
Uterus
Oxytocin
Mammary gland
Prolactin
Skin
MSH
Adipotropins
FSH or LH
ACTH
TSH
GH
Ovary/testes
Adrenal gland
Thyroid
Liver
Adipose tissue
Estradiol
Testosterone
Cortisol
fT_4 or fT_3
IGF1
Adipokines
Cytokines
Free fatty acids
Metabolic function
Proliferation
Differentiation

SUMMARY

- Acute/chronic failure or hyperfunctioning of an endocrine gland can occasionally result in catastrophic illness or death

- It is important to recognizes these abnormalities and manage them appropriately