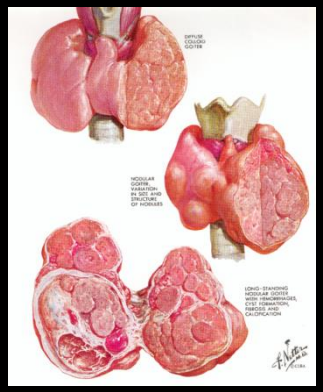
Endocrine Disease in the Elderly



Miles Levy
Consultant Endocrinologist
Leicester Royal Infirmary

BGS Trent Region Autumn Meeting
3rd October 2018

Overview of talk

- Common endocrine incidental findings
- Particular reference to elderly patients
- Things you might come across in real life

Topics covered

- Thyroid
- Sodium
- Pituitary
- Adrenal

Thyroid case

Case 1

- 79 year-old female
- Fall at home
- Weaker than usual
- Paroxysmal AF
- Permanent Pacemaker
- Osteoporosis

Case 1

- Alendronic acid 70mg / week
- Apixaban 5mg
- Amlodipine 10mg
- Furosemide 40mg

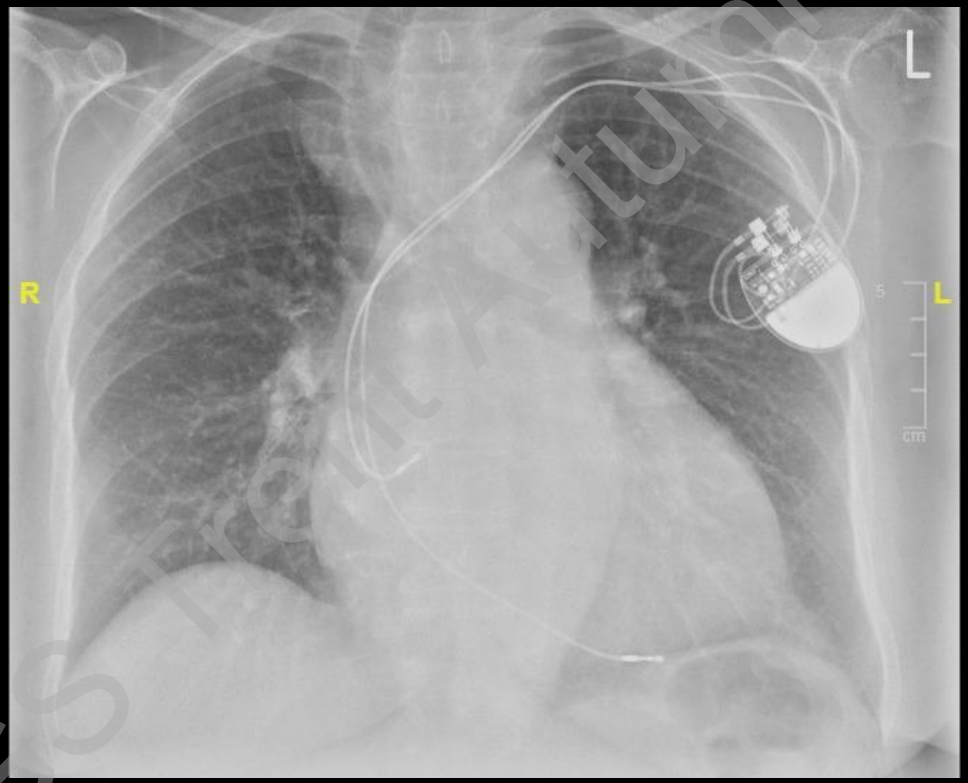
Examination

- Pulse 80/min
- Sinus rhythm
- Not dehydrated
- Proximal muscle weakness
- No other findings

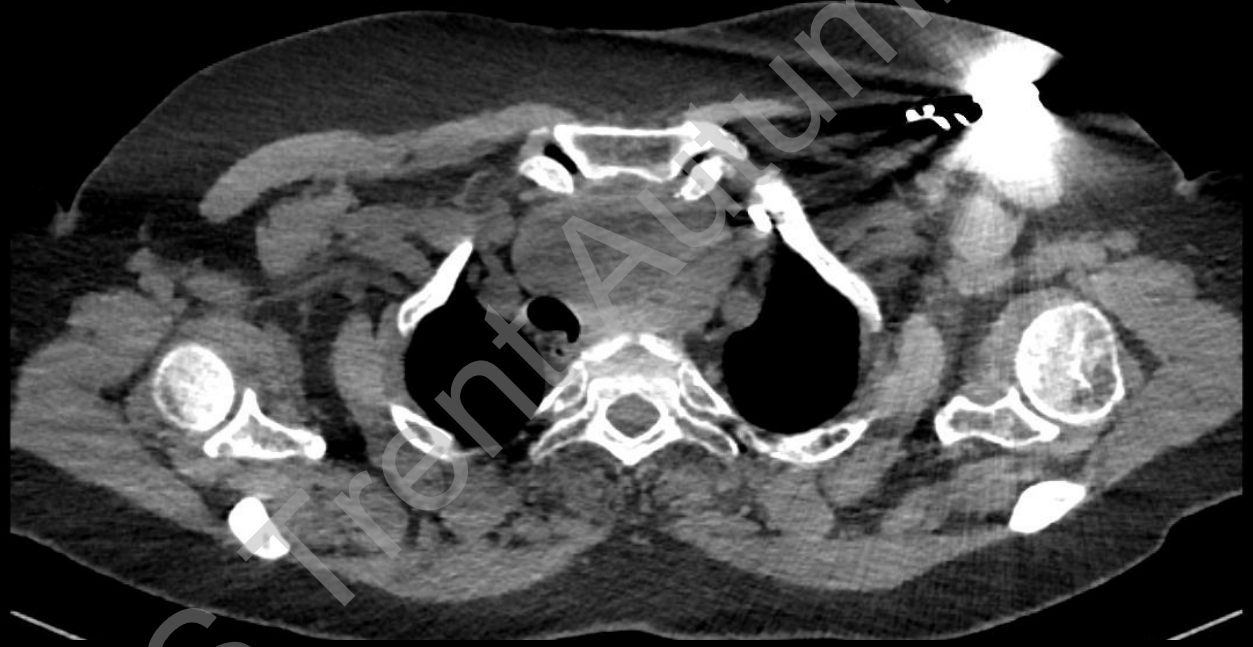
Case 1

- Na 144 mmol/l
- K 3.8 mmol/l
- U 5.2 mmol/l
- C 65 umol/l
- eGFR 81 ml/min
- FBC normal

Chest X-Ray



CT thorax



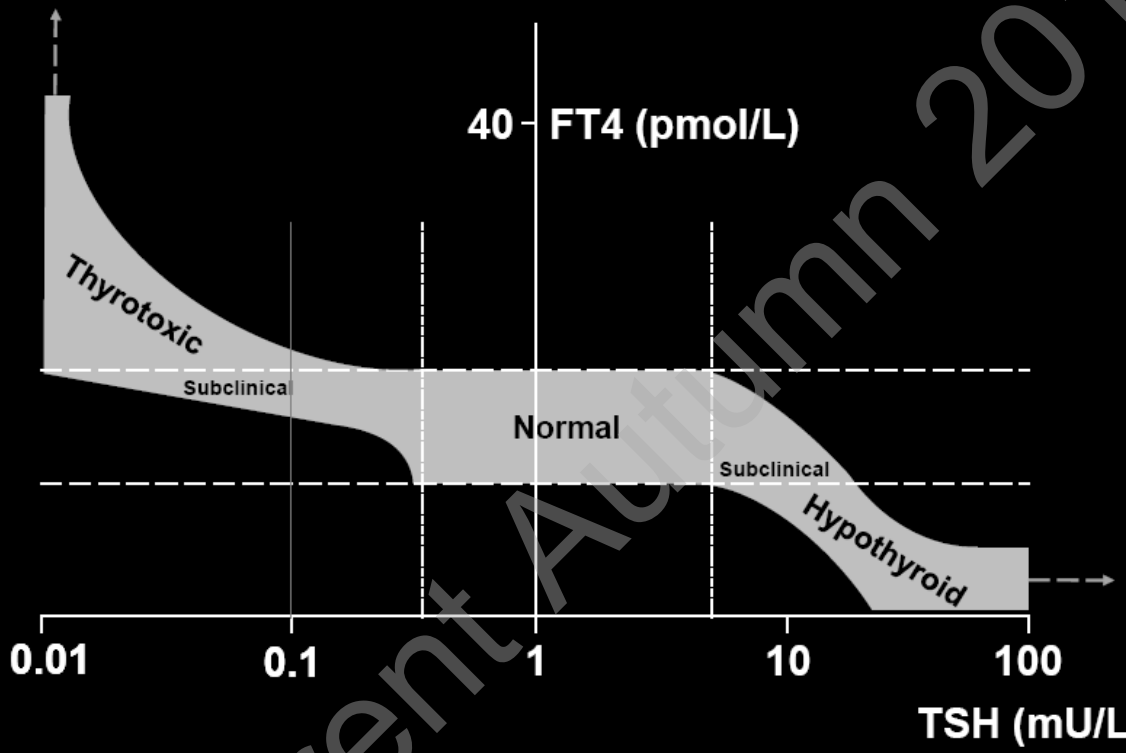
Thyroid function tests

- T4 20 pmol/L (9-25)
- TSH < 0.05 (0.35-5)

Questions

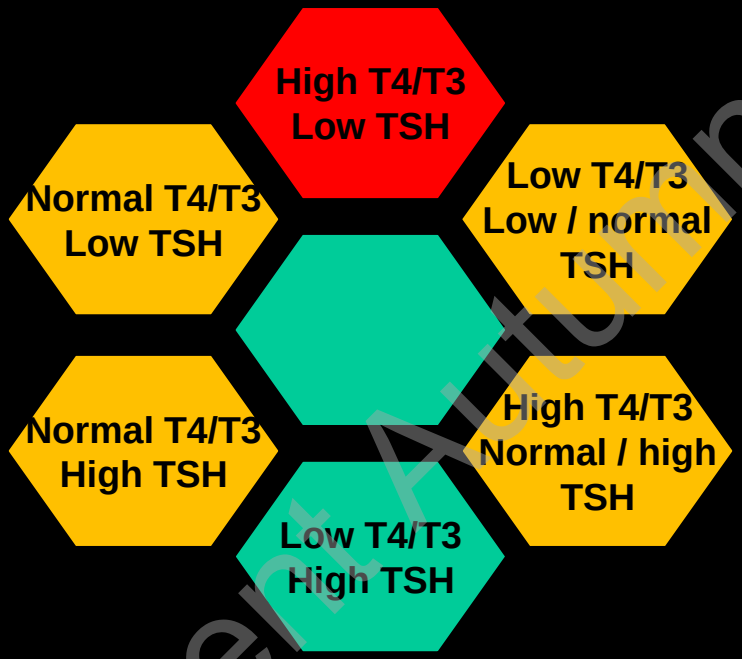
- Should we worry about these TFTs?
- What further investigations are needed?
- Does the patient need to be treated?

Relationship between TSH and FT4



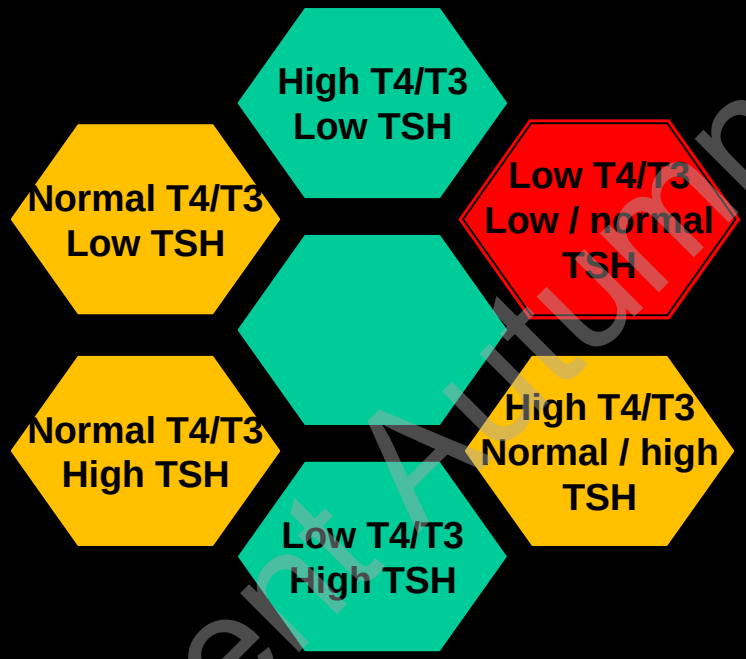
Gurnell *et al*, 2011 *Clin Endocrinol* , 74:673-78.

Causes of a low TSH

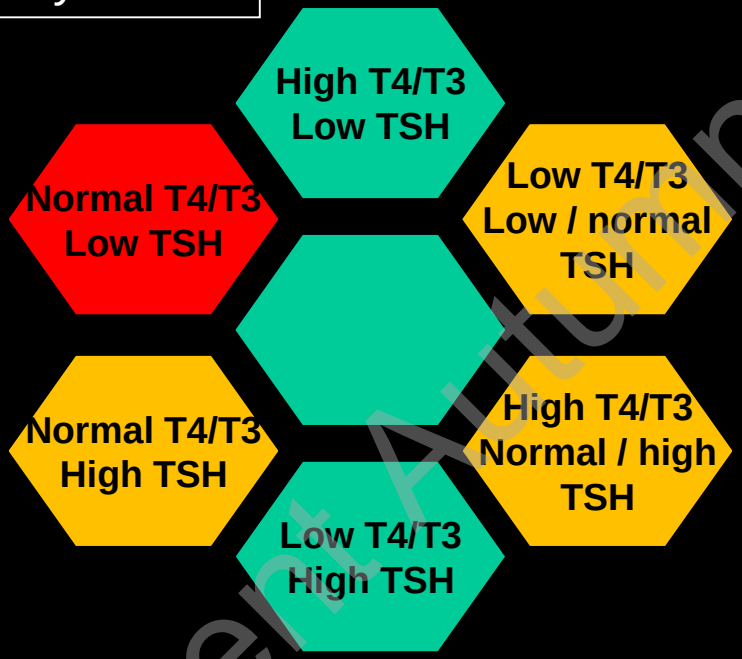


Graves'
Multinodular goitre
Toxic nodule
Thyroiditis
Amiodarone
Excess thyroxine

Central hypothyroidism
Isolated TSH deficiency
Non Thyroid Illness



Sub-clinical hyperthyroidism
Recent treatment hyperthyroidism



Our patient

- T4 20 pmol/L (9-25)
- TSH < 0.05 (0.35-5)
- Unlikely to be sick euthyroid
- LH 80 iU/L, FSH 76 iu/L not hypopituitarism
- T3 6.4 (3.5-6.5) upper normal
- Multinodular goitre

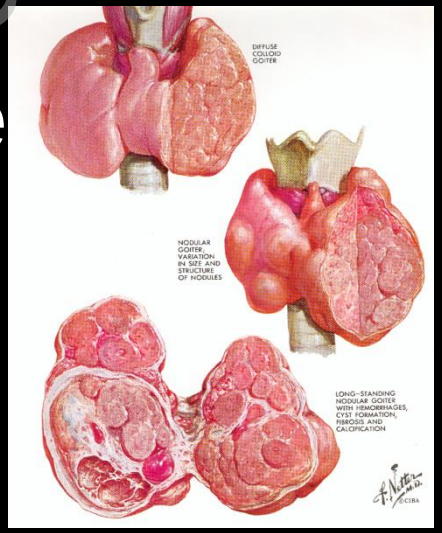
Sub-clinical hyperthyroidism

- Normal T4/T3 with suppressed TSH
- Causes are the same as overt hyperthyroidism

Graves'
Multinodular goitre
Toxic nodule
Thyroiditis
Amiodarone
Excess thyroxine

Sub-clinical hyperthyroidism

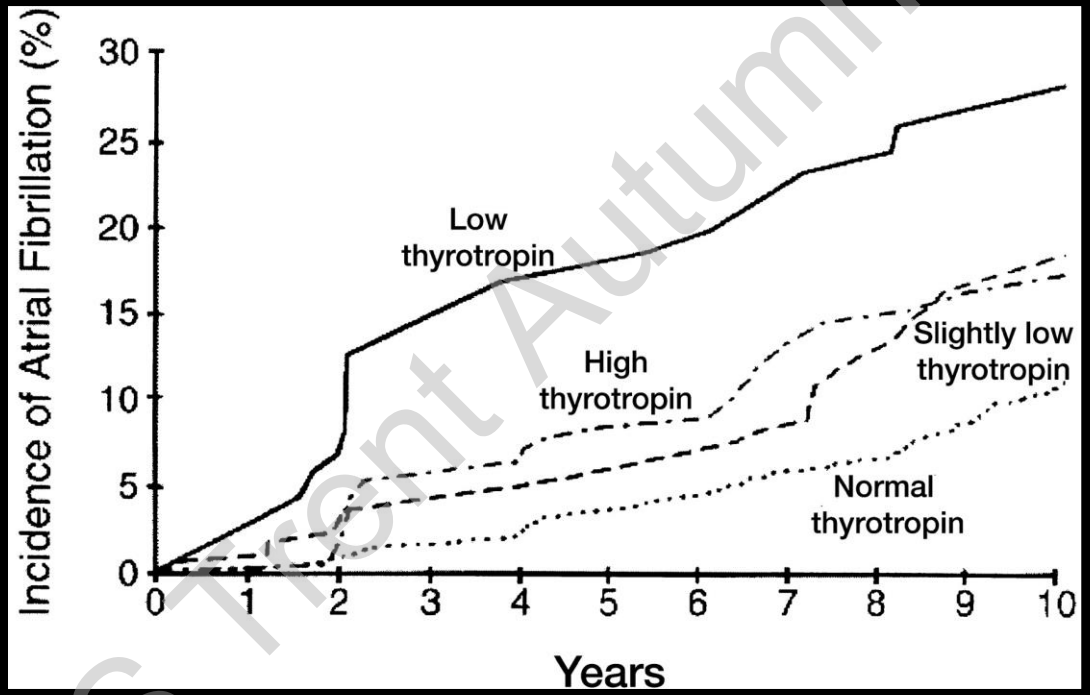
- T3 often at high end of reference range
- Commonly due to autonomous thyroid nodule in the elderly
- Consider auto-immune
- TPO / TSHr Ab



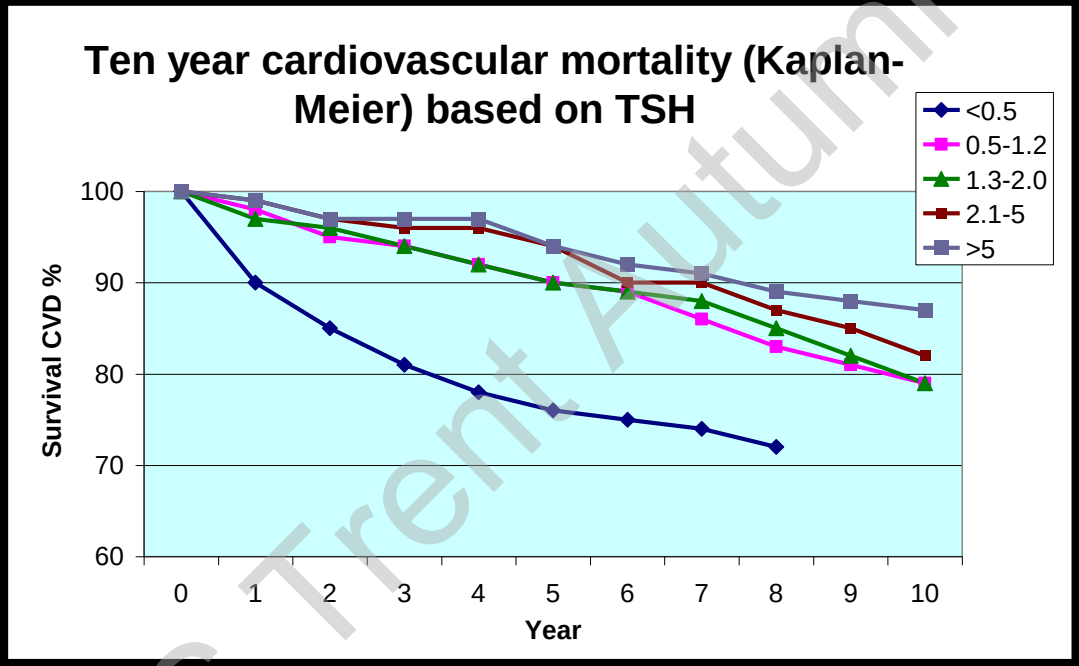
Potential consequences

- Progression to overt hyperthyroidism
- Cardiovascular conditions

Increased risk of AF



Increased Cardiovascular Mortality



Other potential consequences

- Increased risk of osteoporotic fractures[1]
- Increased risk of frailty > 65[2]
- Possible association with dementia[3]

Blum et al., JAMA 2015; 2 Virgini et al. J Clin Endo 2015; 3 Aubert et al Clin Endo 2017

Considerations the elderly

- Older patients are often asymptomatic
- Apathetic thyrotoxicosis
- Proximal myopathy
- Nodular thyroid disease
- Increased CVS risk
- Osteoporosis

Whether to treat

- No randomised trials
- Uncontrolled studies have shown CVS benefit
- In the end it is a clinical judgement call

Our patient

- Repeat TFTs 12 weeks same results
- Trial of carbimazole 10mg
- Improvement in symptoms
- Normalisation of TSH
- Consideration for radio-active iodine

Management of thyrotoxicosis

- Carbimazole or PTU agranulocytosis
- Radio-iodine hypothyroidism / RAI protection
- Surgery laryngeal nerve palsy and hypocalcaemia

Thyroid nodules in elderly

- Very common incidental finding
- Best investigation is ultrasound
- Clinical clues for malignancy and LN
- Anaplastic carcinoma is very rare
- Retrosternal goitres can usually be left

Sodium case

Case 2

- Acute Medical Unit
- 80 year old lady
- Weight loss
- Dizziness
- Unwell

Case 2

- Underweight but not cachectic
- Euvolaemic clinically
- No other findings

Case 2

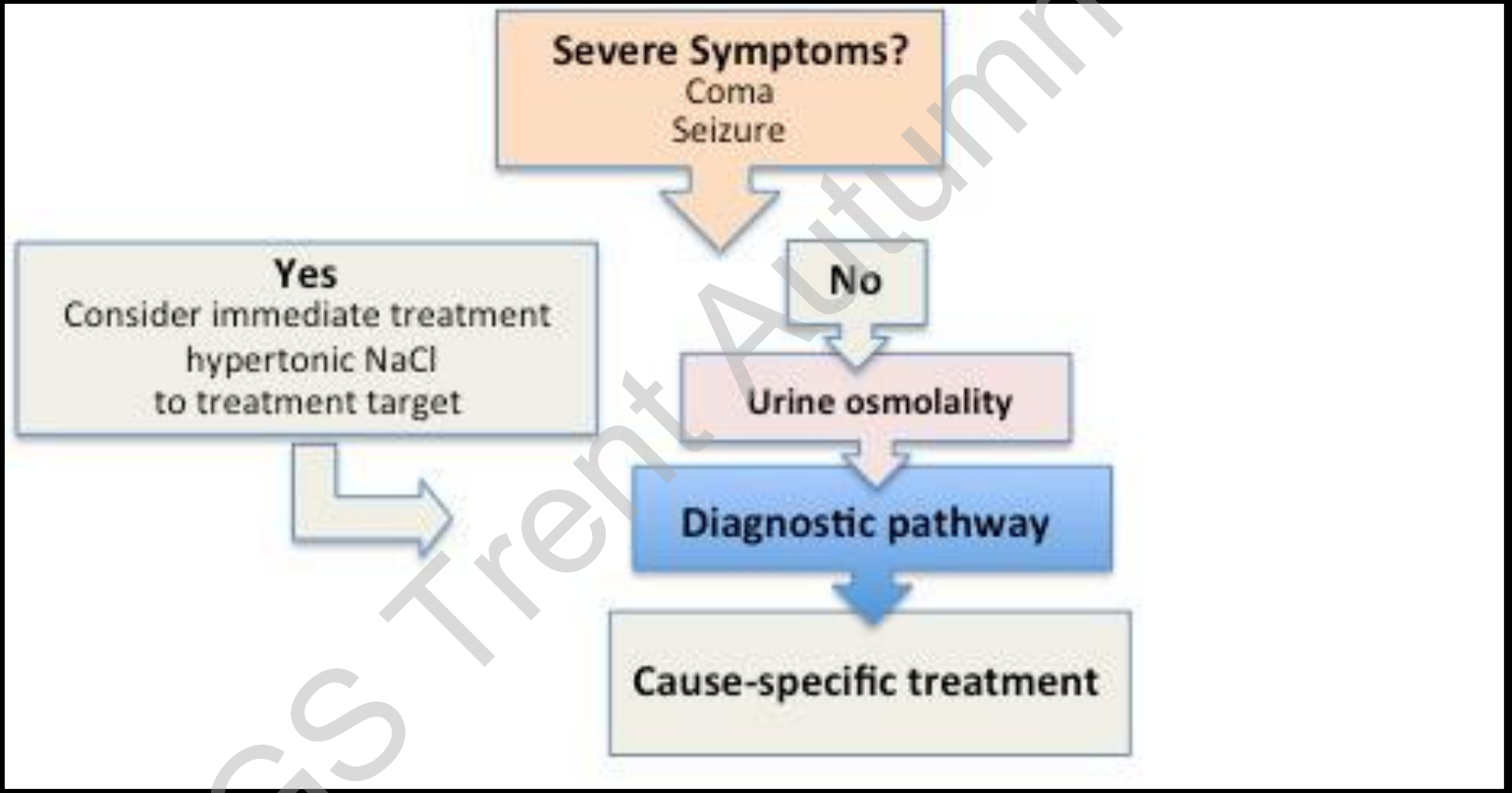
- Na 127 mmol/L mild hyponatraemia
- K 3.8 mmol/L
- U 3.6 mmol/L
- C 49 µmol/L
- CRP < 5
- FBC normal

normal CXR

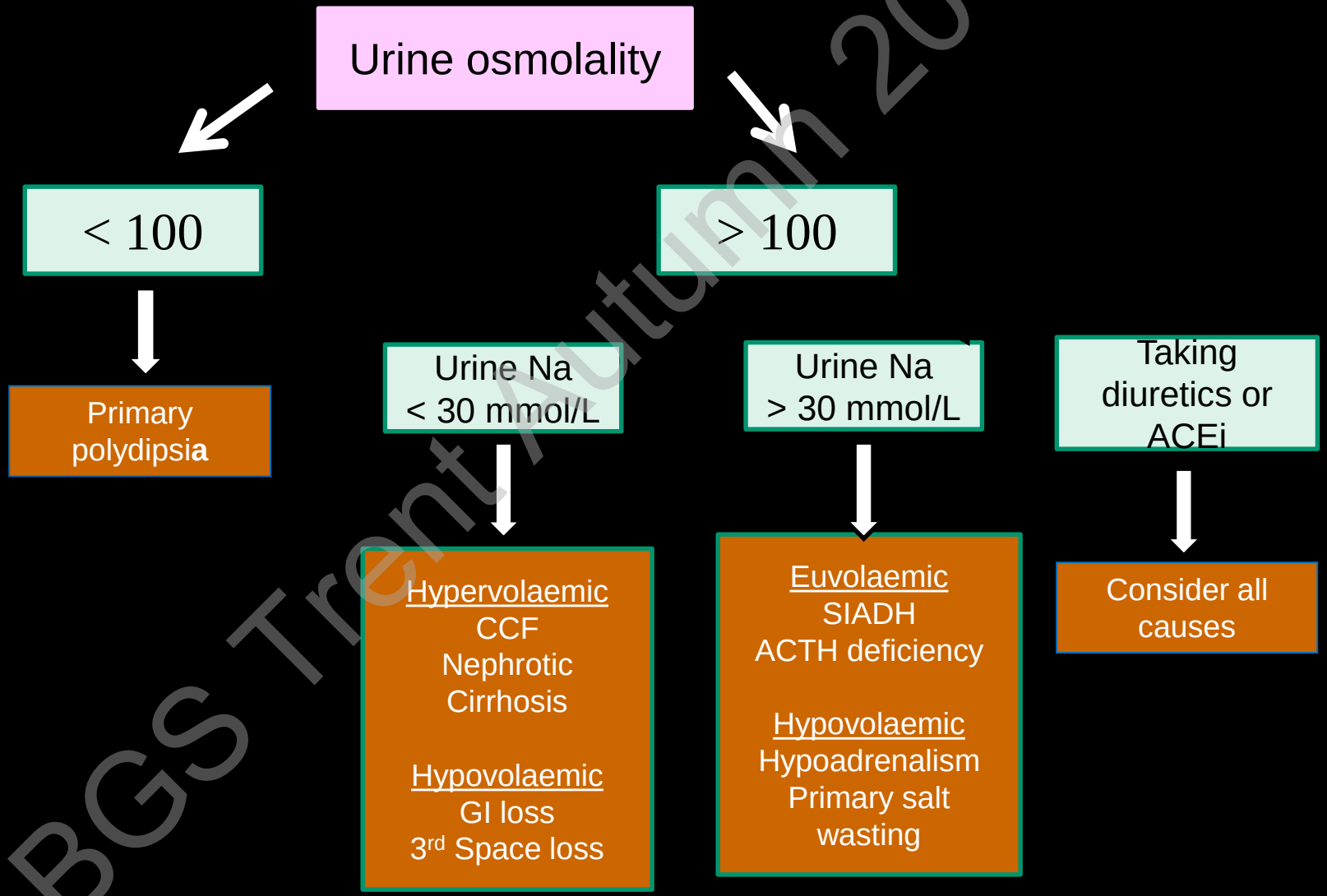
Summary

- 80 year old lady with mild hyponatraemia
- What is the diagnostic approach?
- What are the implications in older people?

Acute severe hyponatraemia v chronic

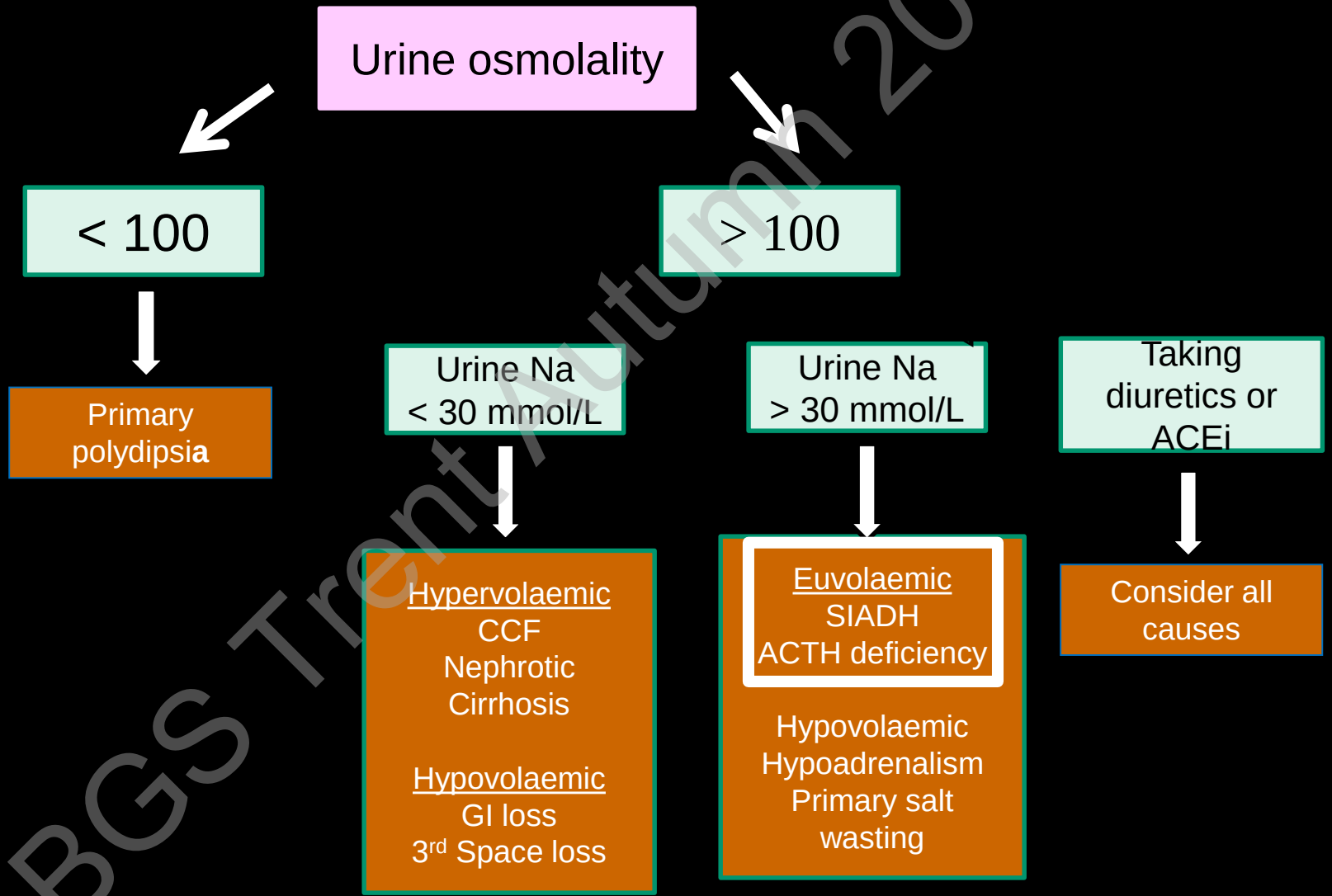


Diagnostic pathway hyponatraemia



Our patient

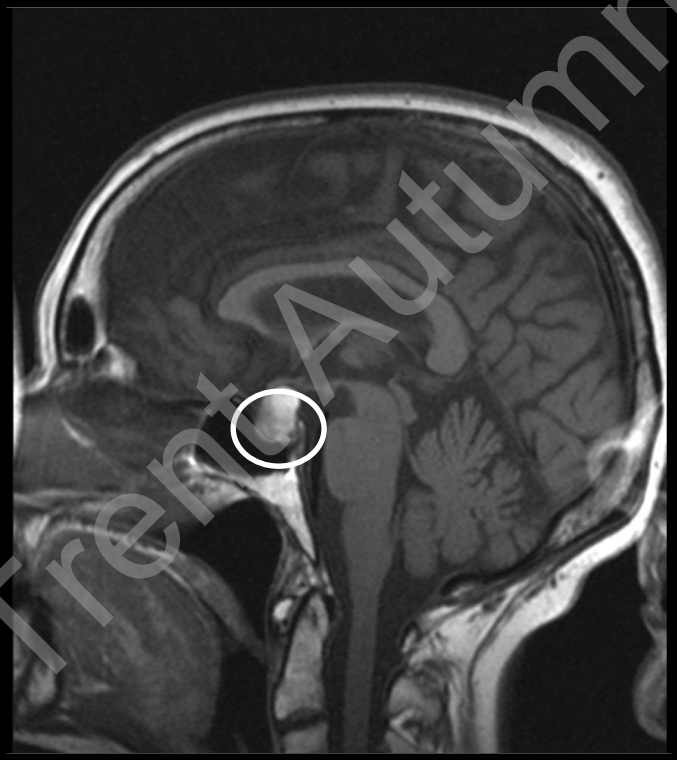
- Serum osmo 256 **low**
- Urine osmo 498 **> 100**
- Urine Na 126 **> 30**



Further investigations

- Cortisol 267 ⟶ 500 nmol/L
- T4 9 pmol/L (9-25)
- TSH 3.7 miU/L (3.5-5)
- LH 1 miU/L
- FSH 2.4 miU/L
- Prolactin 1407 iU/L
- Suggestive of pituitary disease

MRI pituitary fossa



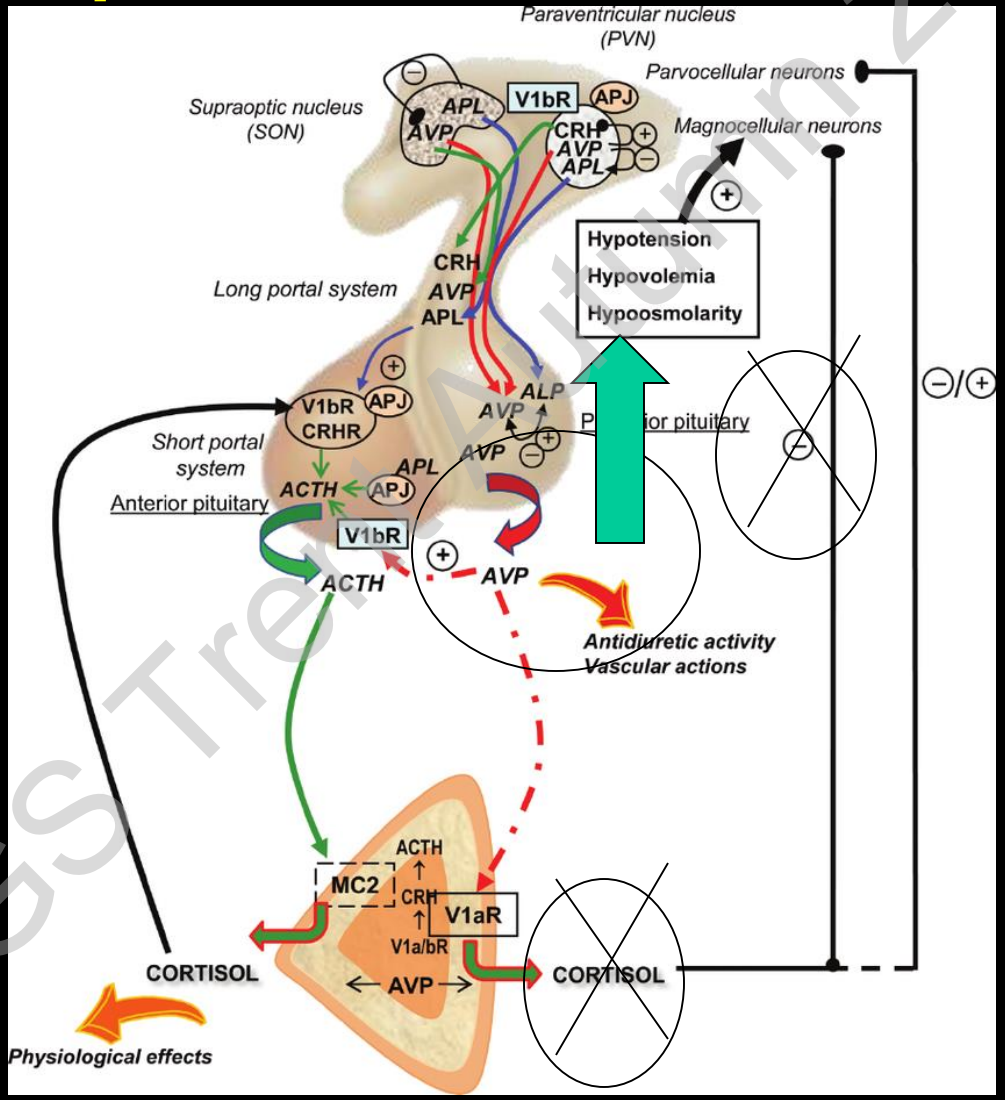
Diagnosis

- Pituitary macro-adenoma
- Hyponatraemia due to ACTH deficiency
- Dramatic improvement on hydrocortisone

Points for discussion

- Hyponatraemia and cortisol deficiency
- Incidental pituitary mass

Vasopressin and cortisol



Hyponatraemia and ACTH deficiency

- Looks identical to SIADH
- Different to mechanism of hyponatraemaia in Addison's disease (mineralocorticoid)

Hyperkalaemia and pigmentation

Clinical relevance in elderly

- Do not assume diagnosis of SIADH
- Treatment with hydrocortisone life-changing
- Consider ACTH suppression in all hyponatraemic patients on prednisolone
- Increase steroid dose during inter-current illness or consider parenteral adminstration

Hyponatraemia in the elderly

- 30% of all in-patients
- Increased recognition of morbidity
- Associated with increased risk of falls
- Increased osteoporosis and fractures
- Impaired cognition and co-ordination

Corona et al. Clin Endo 2018

Incidental pituitary mass

Pituitary incidentaloma

Small low density lesion in pituitary gland
< 1cm diameter

Pituitary Micro-adenoma

- Very common
- Up to 1 in 10 MRI scans
- No need for dynamic endocrine assessment

Approach to pituitary micro-adenoma

- Consider clinical evidence of hyper-secretion
- Basal pituitary blood tests

Biochemical test for acromegaly

- Oral Glucose Tolerance Test
- GH suppresses < 1µg/L in normals
- Elevated serum IGF-1 level

Biochemical test for Cushing's

- 24h urine free cortisol
- Overnight dexamethasone suppression test
- Low dose dexamethasone suppression test
- Cortisol < 50nmol/L

Basal pituitary function tests

- LH / FSH / testo in men
- LH / FSH / E2 in women
- Prolactin
- fT4 / TSH
- GH / IGF-1
- 0900 cortisol

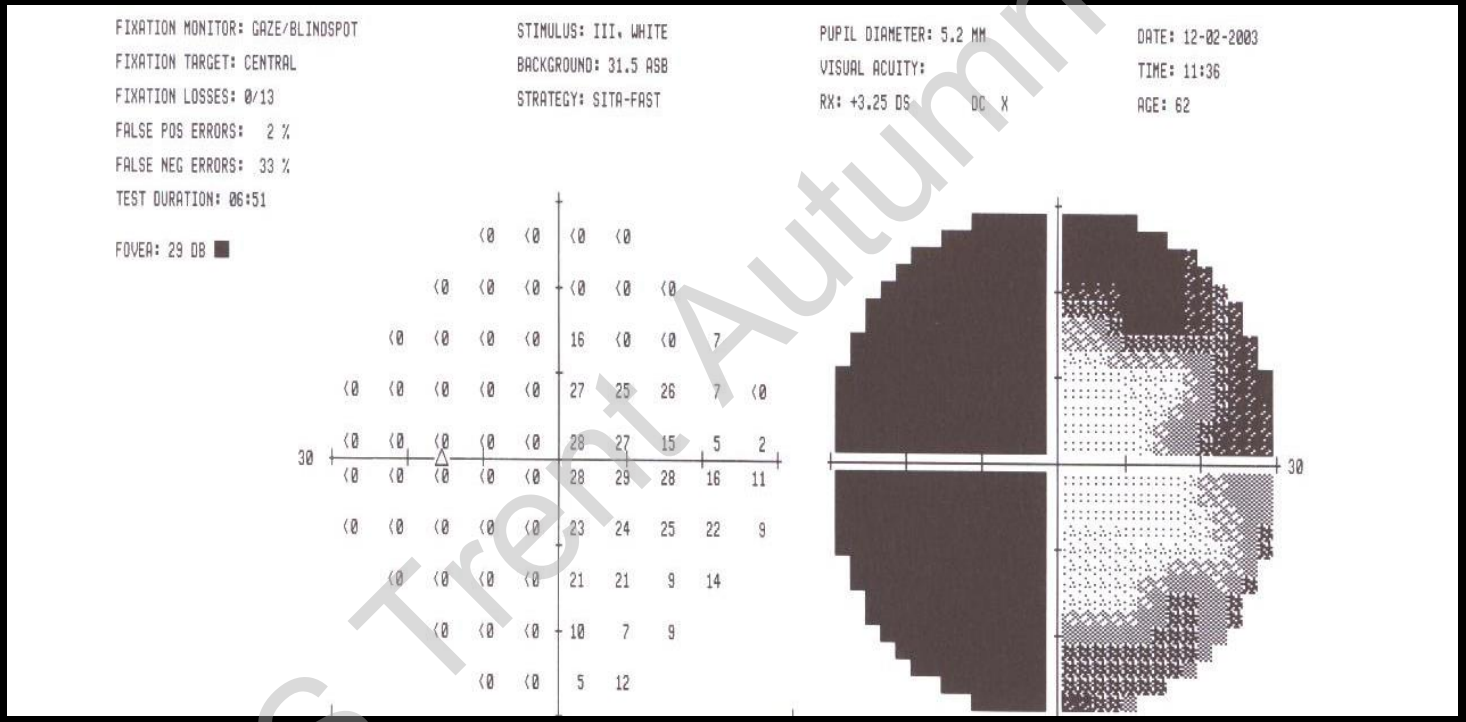
Pituitary Macro-adenoma

1cm diameter

Pituitary Macro-adenoma

- 1 in 500 MRI scans
- Visual field assessment
- Consider acromegaly and Cushing's
- Basal pituitary blood tests
- Dynamic assessment of reserve
- Follow up imaging in 12 months

Temporal visual field loss



Dynamic pituitary assessment

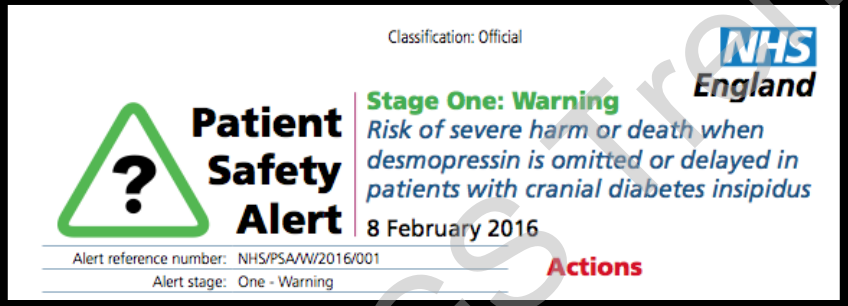
- Cortisol status synacthen test
- GH reserve glucagon stimulation test
- Easily done in endocrine unit
- GH replacement may improve quality of life

In-patients with hypopituitarism

- Hydrocortisone may need IM or IV
- Thyroxine no need to change dose
- Growth hormone OK to omit
- Desmopressin vital not to omit

Desmopressin during intercurrent illness

- Synthetic vasopressin (DDAVP)
- Treatment of Cranial Diabetes Insipidus
- Severe dehydration and hypernatraemia
- Preventable deaths reported



Classification: Official

NHS England

Patient Safety Alert

Stage One: Warning

Risk of severe harm or death when desmopressin is omitted or delayed in patients with cranial diabetes insipidus

8 February 2016

Alert reference number: NHS/PSA/W/2016/001

Alert stage: One - Warning

Actions

make sure patients with DI get desmopressin and fluids

Hypernatraemia in the elderly

- Strong association with frailty
- Suggests profound water deficit
- Poor prognostic sign
- Fluid balance is key
- Always consider DI

Urine volume > 3L / 24 h
Urine osmolality < 600

Adrenal cases

Case 3

48 year old lady

CTPA for suspected PE

No previous history

PE excluded

1.5cm left adrenal lesion

Questions

Is this a concern?

Are any tests needed?

Is a follow up scan required?

Adrenal incidentaloma

Very common (3-10%)

Sensible guidelines[1]

< 4cm in diameter

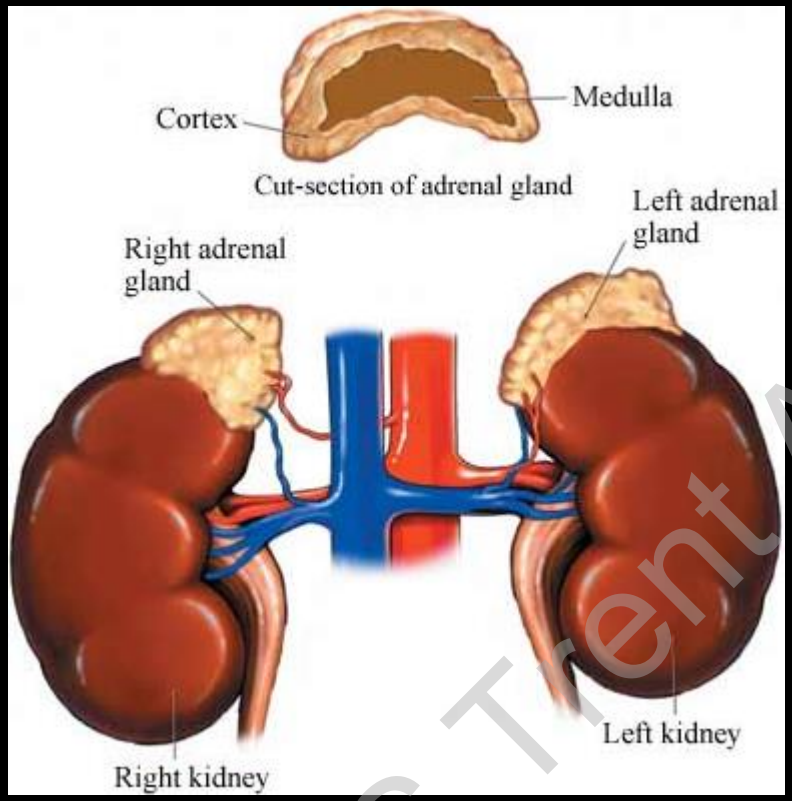
Radiologically benign

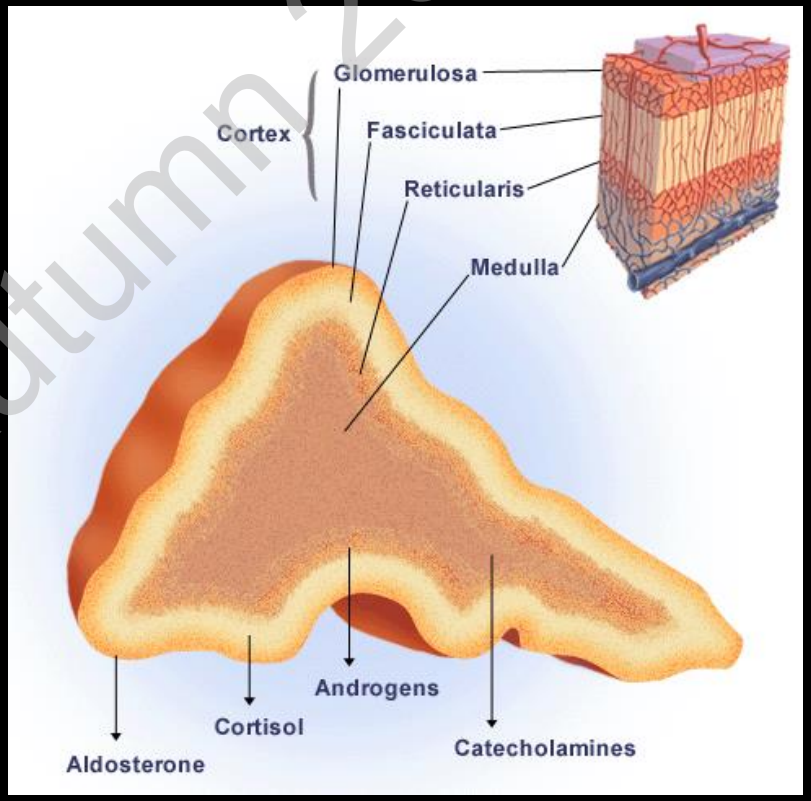
Non-functional

Can discharge patient

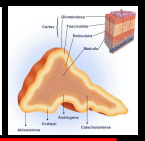
1 Fassnacht et al. *ESE* 2016

Quick revision of adrenal gland





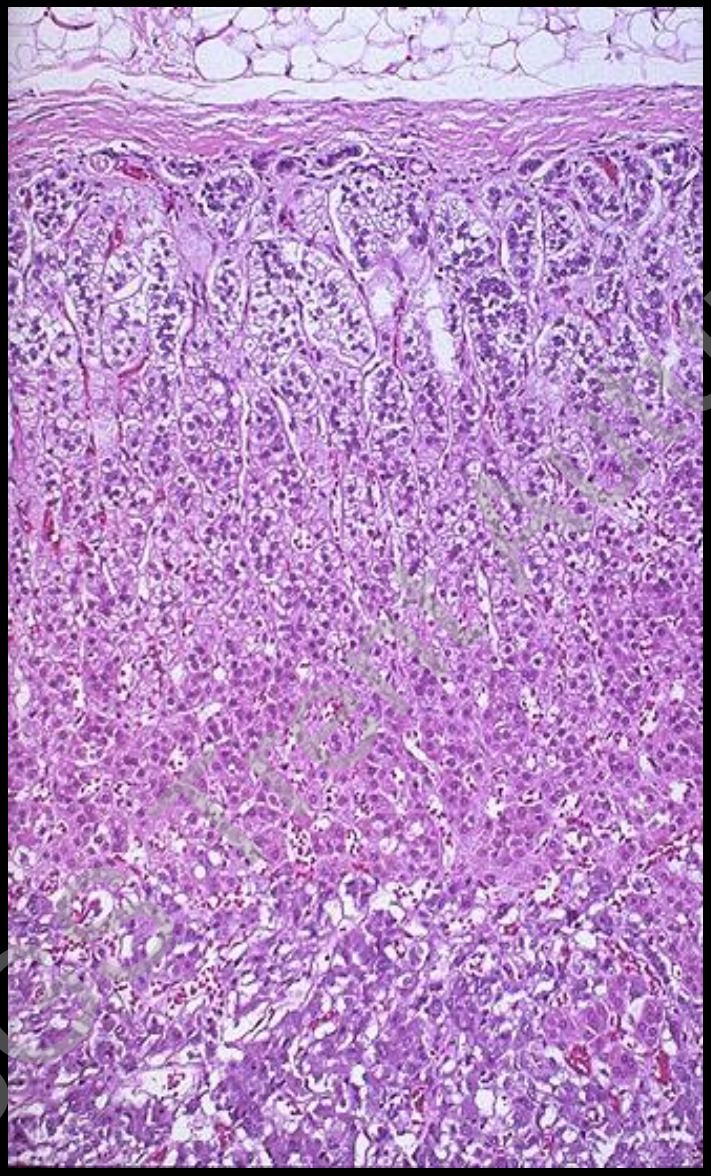
Normal adrenal histology



ZG

ZF

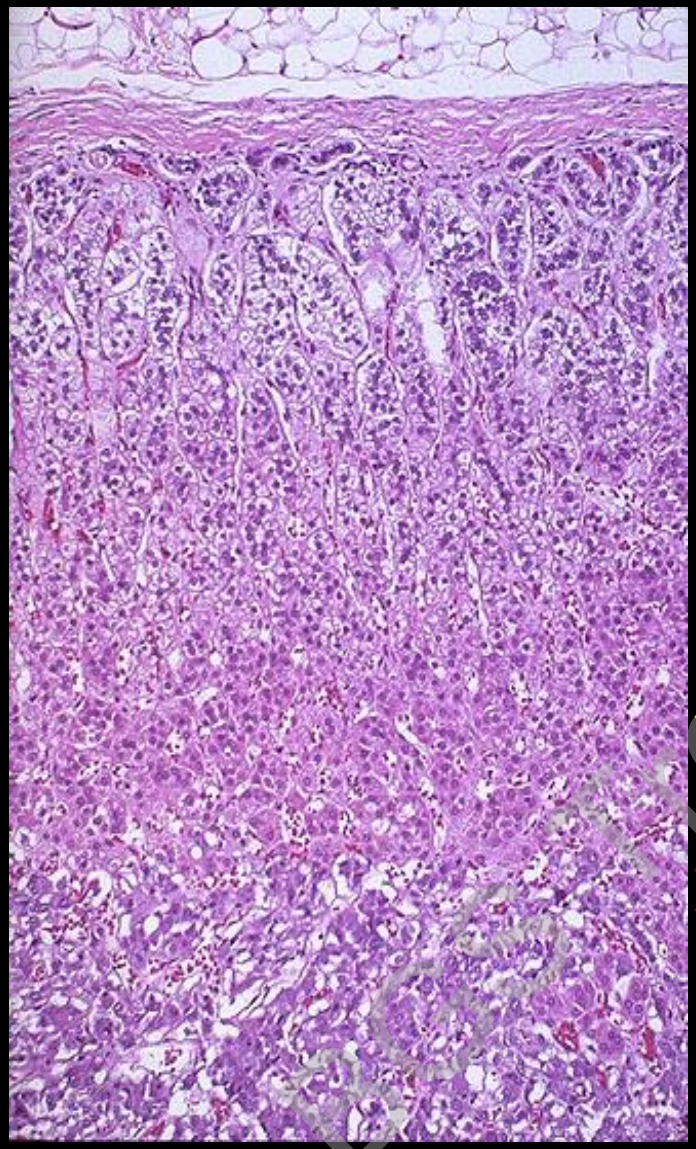
ZR



Adrenal Cortex

Adrenal Medulla

Biochemical tests



Cortex

ZG

Primary hyperaldosteronism
Hypertension and hypokalaemia

ZF

Cushing's syndrome
Autonomous cortisol secretion

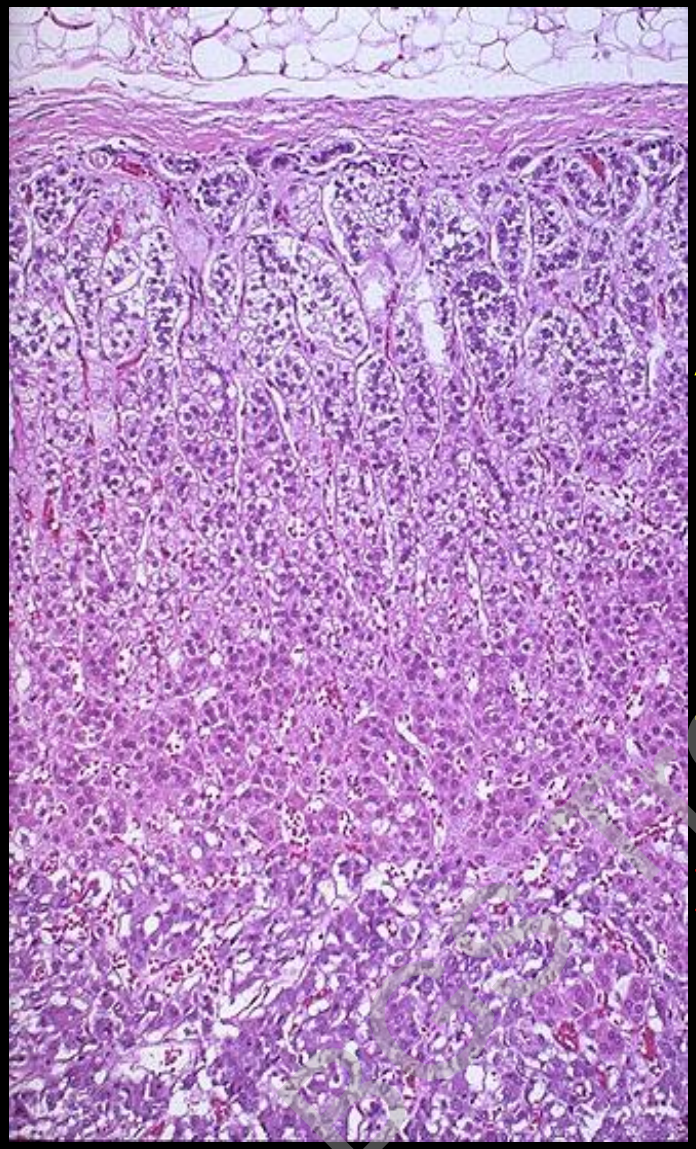
ZR

Virilisation in a female
Gynaecomastia in a male

Medulla

Catecholamine excess
Suspicion of phaeochromocytoma

Biochemical tests



Cortex

ZG

Blood pressure, serum potassium
Aldosterone / renin ratio

ZF

24h UFC
Dexamethasone Suppression Test

ZR

Testosterone
17-Hydroxyprogesterone

Medulla

24h urine catecholamines
Metanephrines

Radiology for adrenals

Non-contrast CT adrenals

Fatty lumps benign and homogenous

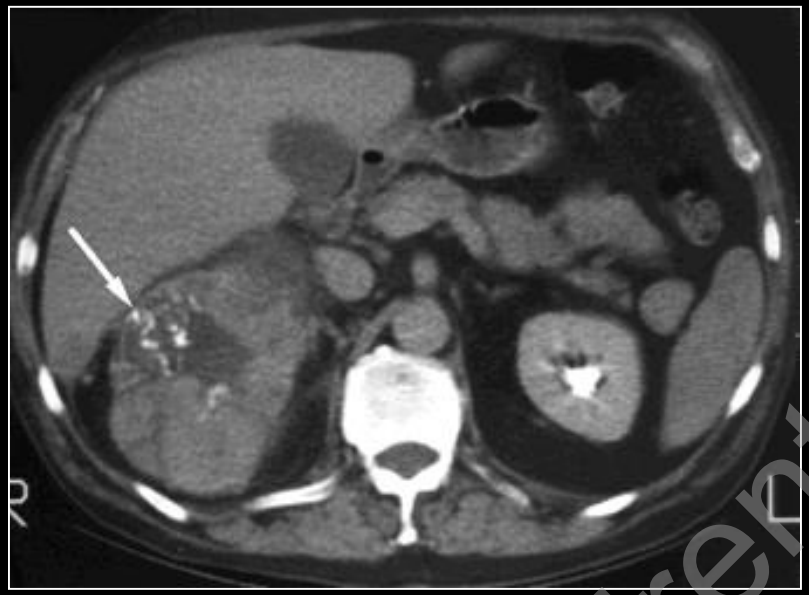
Low intensity on CT Hounsfield Units < 10

If indeterminate then options are

- Different scan straight away contrast-enhanced washout CT or MRI
- Repeat imaging in 6-12 months

No real role for adrenal biopsy unless cancer elsewhere

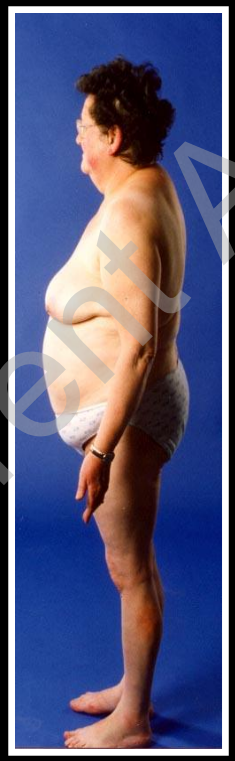
Non-benign looking lesions



Screening for cortisol secretion

Overt Cushing's syndrome

Not Cushingoid in appearance



Biochemical screening for Cushing's

1mg overnight dexamethasone suppression test

Cortisol < 50 nmol/L is normal

Cortisol 51-138nmol/L is possibly not

'Possible autonomous cortisol secretion'

Possible autonomous cortisol secretion

Previously called ‘sub-clinical Cushing’s

Seems to be associated with cardiovascular risk

A relative indication for surgery

Probably warrant follow up

Watch this space…..

Case 4

73 year old lady

Abdominal discomfort and bloating

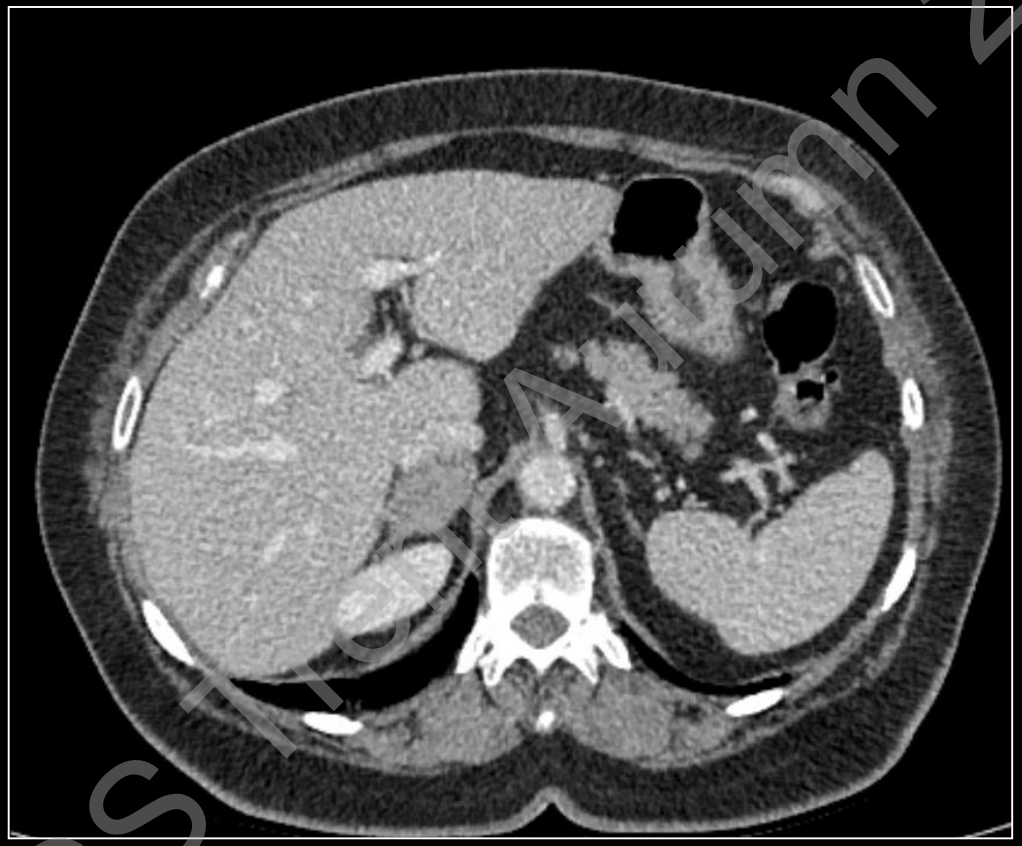
Bowel cancer screening FOB +ve

Colonoscopy showed R colonic tumour biopsy malignant

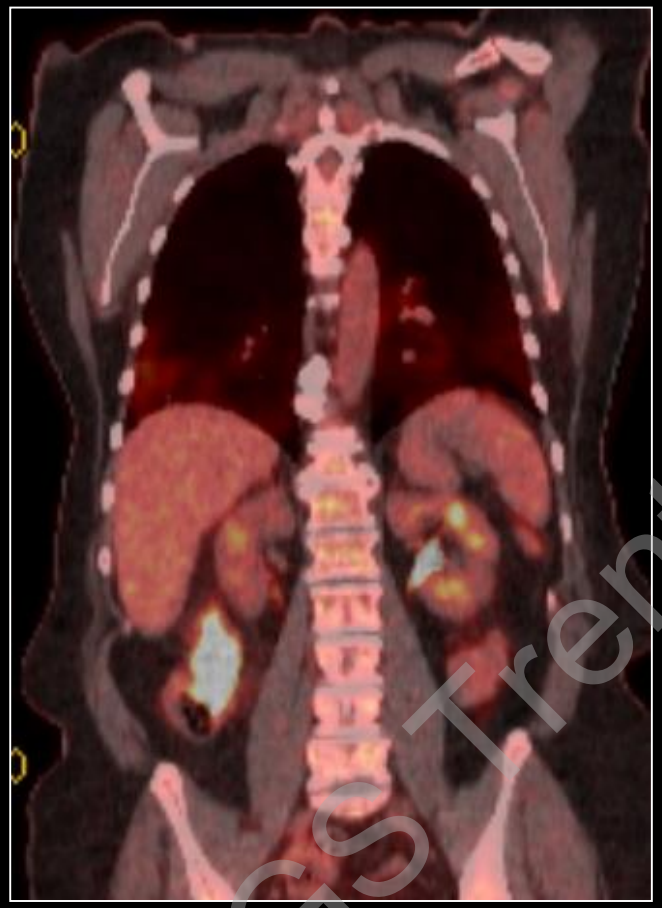
CT scan 3.6cm right adrenal mass

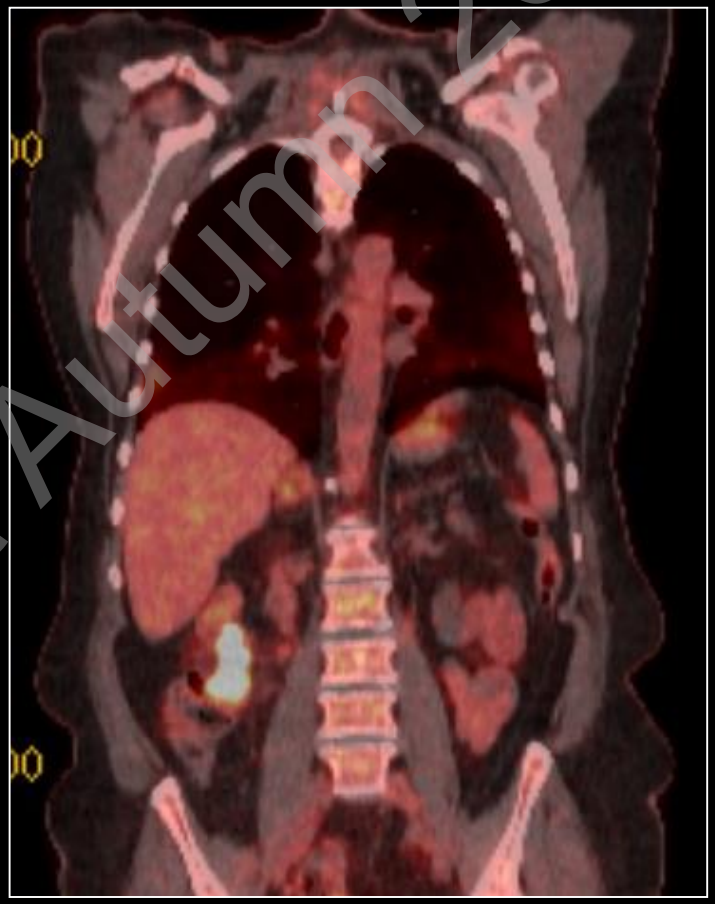
Due for surgery next week

CT scan



FDG-PET





Questions

What is the single most important test before operation?

Should the adrenal gland be removed at the same time?

Questions

Indication for rapid turnaround for plasma metanephrines

10/03/2018 04:30 Urine
Request Reason : adrenal mass, cancer of large bowel

24Hr Urine creatinine	7.6	mmol/24hr	(5 to 17)	Auth
Normetadrenaline	1.37	umol/24hr	(0.00 to 3.00)	Auth
Metadrenaline	0.35	umol/24hr	(0.00 to 1.00)	Auth
Total Metanephrine	1.72	umol/24hr	(0.00 to 4.00)	Auth
3-Methoxy Tyramine	0.68	umol/24 hrs	(0.00 to 2.30)	Auth

Comments :
All metanephrines and 3-methoxytyramine are within their reference ranges. Phaeochromocytoma is unlikely.
Repeat testing or further investigations may be indicated if there is a strong clinical suspicion of phaeochromocytoma.

5-OH indoleacetic acid	17	umol/24hr	(0 to 40)	Auth
HMMA (VMA)	22	umol/24hr	(0 to 40)	Auth

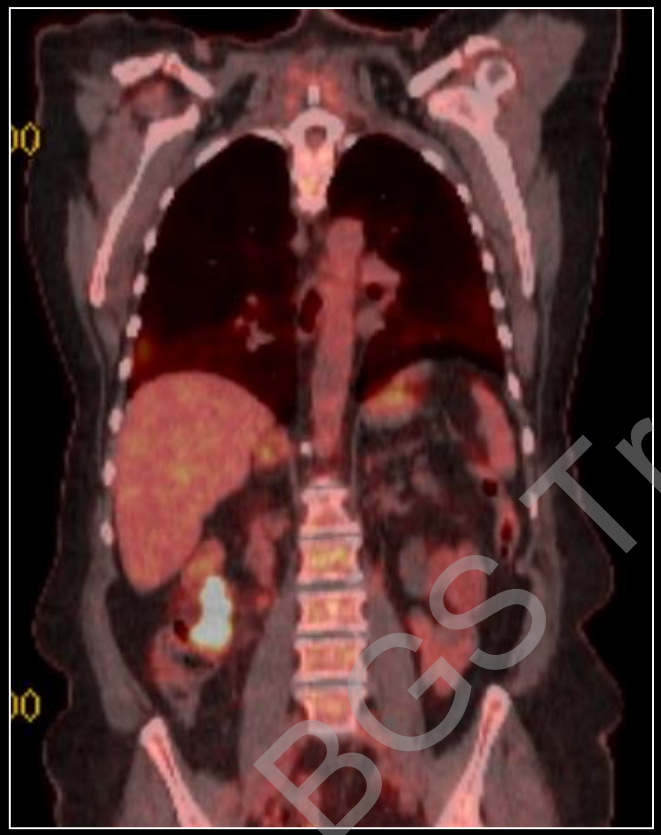
13/03/2018 08:55 Serum
Specimen Comment : POST DOSE
Request Reason : ADRENAL MASS

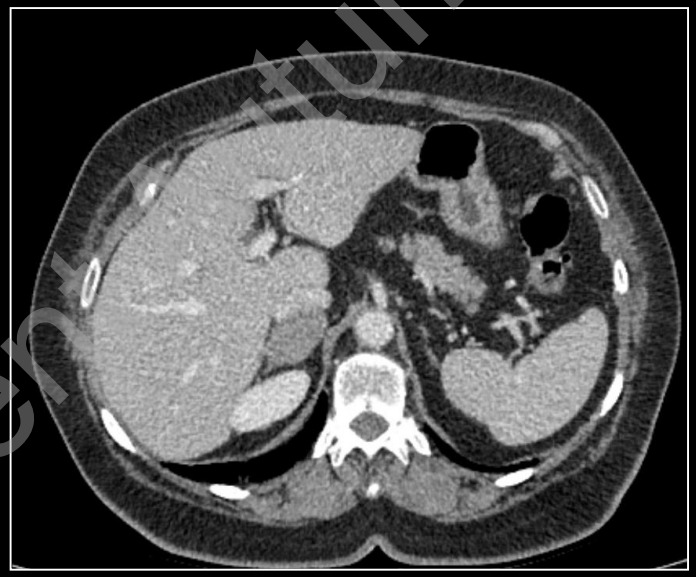
Cortisol	45	nmol/L	Auth

Questions

What is the single most important test before operation?

Should the adrenal gland be removed at the same time?





Deal with it later
Bowel cancer priority

Case 5

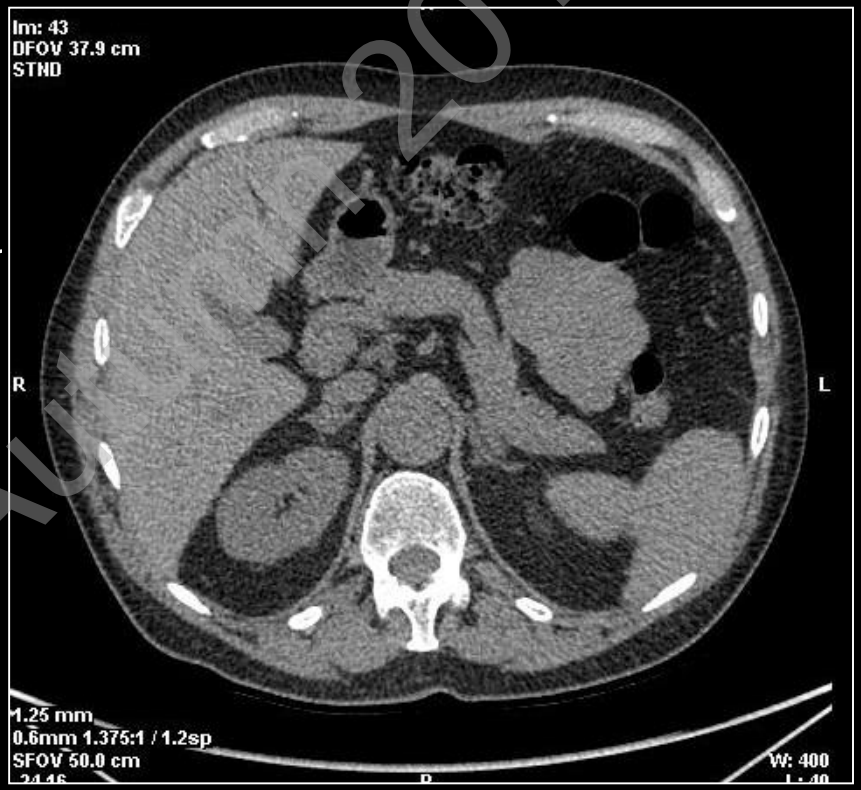
67 year old male

Hypotension and hypokalaemia

K+ 2.7 mmol/l

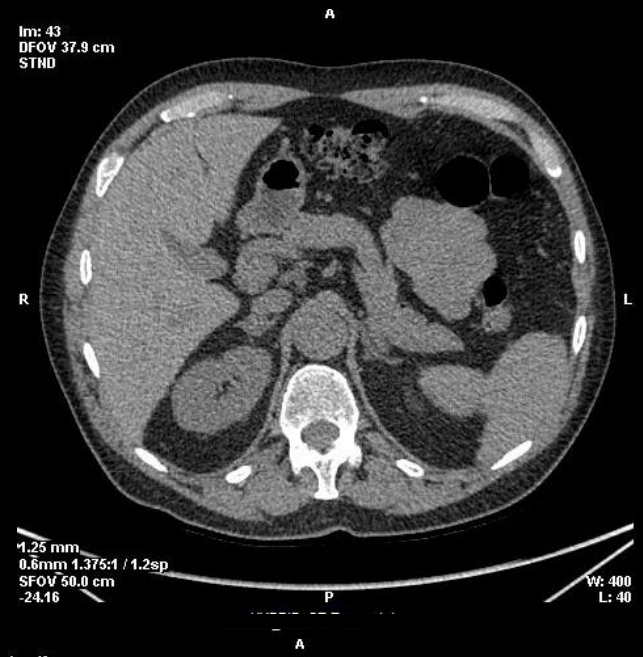
Aldosterone 902 pmol/L

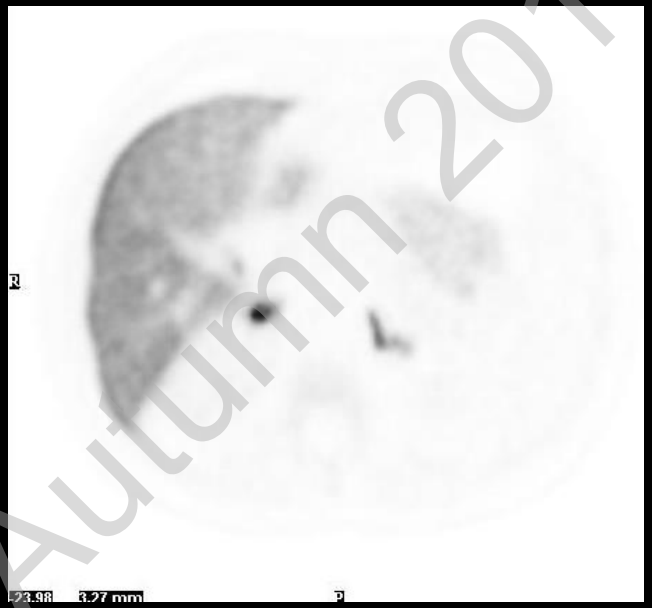
Renin 4 mU/L

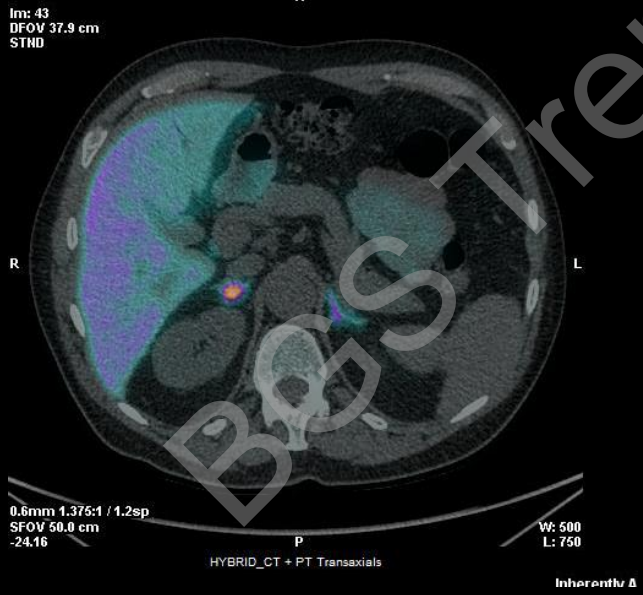


CT bilateral adrenal nodules

Metomidate PET scan







Adrenal Vein Sampling:

AVS 16/2/2018	Aldosterone	Cortisol	A/C ratio
3. Right Adrenal V.	360000	39596	9.09
4. Right Adrenal V.	198000	41636	4.76
2. Left Adrenal V.	3690	4002	0.92
1. Left Adrenal V.	3630	2348	1.55
7. Low IVC	2910	973	2.99
6. High IVC	4680	1270	3.69

Case 5

Right Conn's adenoma

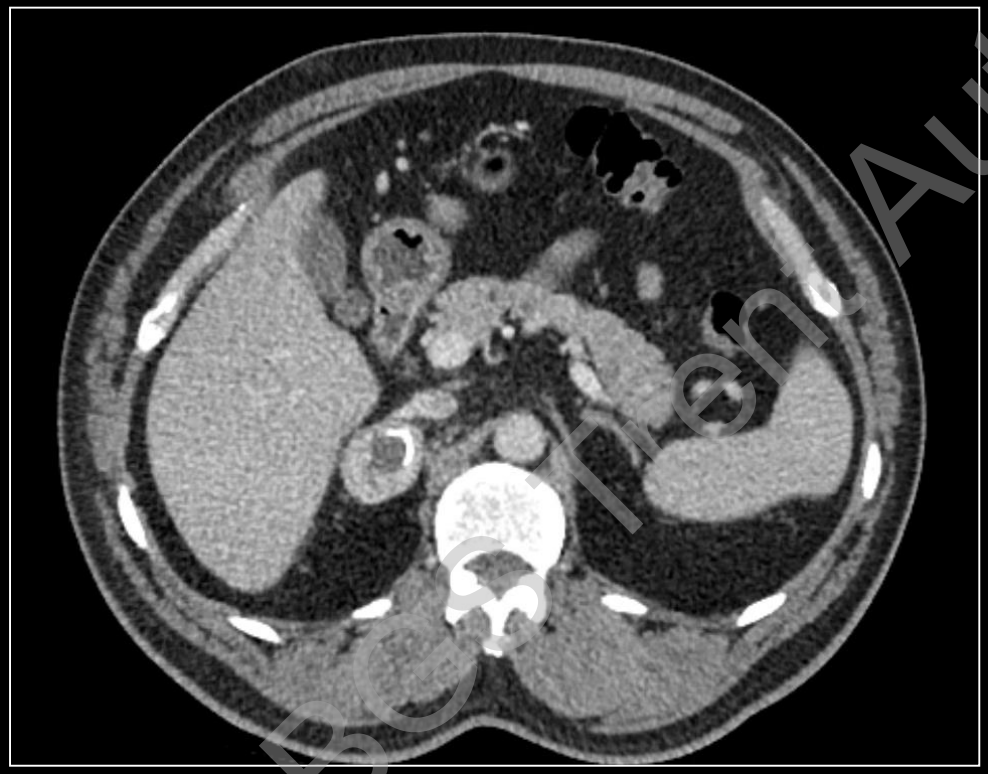
Functional imaging helpful

Referred for surgery

Case 6

78 year old man

Weight loss and muscle weakness



3.7cm right adrenal mass

Calcification and cystic centre

Case 6

09/11/2017 09:15 Urine
Request Reason : adrenal adenoma

Normetadrenaline	8.64	umol/24hr	(0.00 to 3.00)	Auth
Metadrenaline	0.92	umol/24hr	(0.00 to 1.00)	Auth
Total Metanephrine	9.56	umol/24hr	(0.00 to 4.00)	Auth
3-Methoxy Tyramine	1.09	umol/24 hrs	(0.00 to 2.30)	Auth

Comments :
Raised urine metanephrines, phaeochromocytoma is possible.
False positive increases in urine metanephrines can occur with drugs such as tricyclic antidepressants and monoamine oxidase inhibitors.
Diet rich in bananas, pineapples, nuts and caffeine may also raise levels.
Suggest repeat sample avoiding catecholamine rich food and, if possible, the above mentioned medications for 7 days. Please provide complete drug history.

24h urine

06/11/2017 10:20 Plasma
Request Reason : Adrenal adenoma

Plasma Metanephrine	178.0	pmol/L	(0.0 to 510.0)	Auth
Plasma Normetanephrine	2191.3	pmol/L	(0.0 to 1180.0)	Auth

Comments :
Raised plasma normetanephrine.
Suggest send repeat sample after overnight fast and 15 minutes recumbent position.

Plasma 3-Methoxytyramine	<75.0	pmol/L	(0.0 to 180.0)	Auth

Plasma

Case 6

Phaeochromocytoma

Alpha-Blockade

Beta-Blockade

Adrenalectomy

Case 7

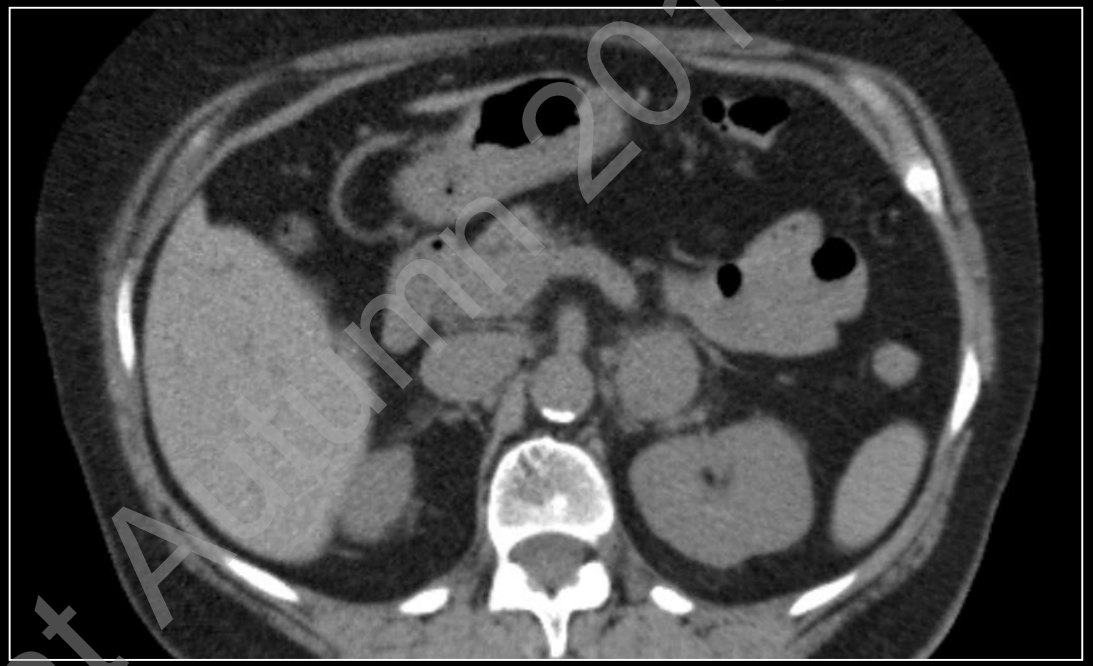
75 year old lady

Hypertension

Type 2 Diabetes

Ischaemic Heart Disease

Not Cushingoid



3cm left adrenal mass

Case 7

Plasma metanephrines normal

24h UFC normal

Post-dex cortisol 322 nmo/L autonomous cortisol secretion

ACTH 6 (low-ish)

Case 7

Slight increase in size of adrenal mass

Diabetes and hypertension worse

Laparoscopic adrenalectomy

Significant improvement diabetes, BP, weight

Reduction in cardiovascular risk

Probably Cushing's syndrome

Adrenal incidentaloma summary

Very common (3-10%)

Sensible guidelines[1]

< 4cm in diameter

Radiologically benign

Non-functional

Can discharge patient

1 Fassnacht et al. *ESE* 2016

Topics covered

- Thyroid — Sub-clinical hyperthyroidism and nodules
- Sodium — Approach to investigation
- Pituitary
- Adrenal

} Investigation of incidental mass

Overview of talk

- Common endocrine incidental findings
- Particular reference to elderly patients
- Things you might come across in real life

The End