

# Endocrine tests

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# Lecture Outline

1. Case
2. Audience interaction
3. Take-home messages

# Interactive keypads



- Slide the power switch up (I = ON)
- Press 
- Press 
- You should now be connected **ANS:**

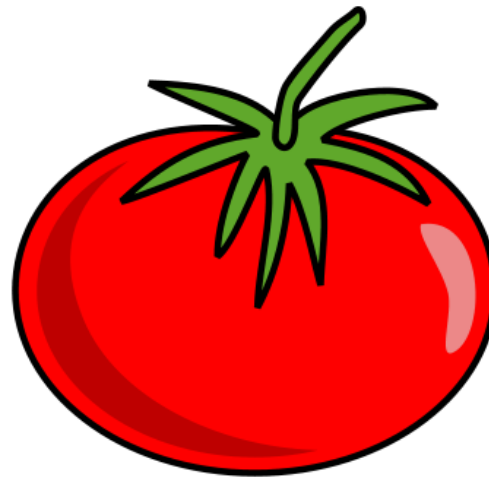
# What colour are bananas?

- A. Blue
- B. Pink
- C. Yellow
- D. Red
- E. Black



# What colour are tomatoes?

- A. Blue
- B. Pink
- C. Yellow
- D. Red
- E. Black



# **27 year old female attends with missed periods for last 5 months**

Previous menses regular (28 day cycle)

No FH of early menopause

PMH: coeliac disease

## **O/E**

Normal secondary sexual characteristics

Not hirsute

BMI 18kg/m<sup>2</sup>

# What would you do first?

- A. Endocrine referral
- B. Pregnancy test
- C. Prolactin
- D. Serum testosterone
- E. Ask her to wait one further month to see if they restart

# Initial biochemical work up

- Pregnancy testing
- LH/FSH
- Prolactin
- TSH



# Results

- TSH 2.40 (normal range 0.30 – 4.20 mu/L)
- T4 14 (normal range 9 – 23 pmol/L)
- Prolactin **1016** (normal range 100 – 500 mIU/L)
- LH **1.0** (Female follicular: 2-10, Female mid-cycle: 20-60, Female luteal: 4-14, Female post-menopause: >20)
- FSH 2.0 (Female follicular : 1.5-10, mid-cycle : 7-20, luteal : 1.5-8, post-menopause : >20)

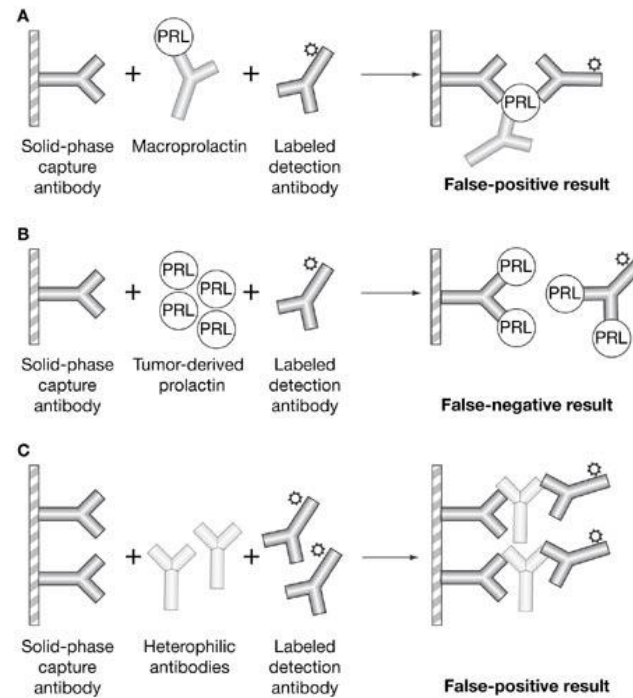
# What next?

- A. Endocrine referral ?prolactinoma
- B. Arrange repeat tests after one week interval
- C. Await macroprolactin screen result
- D. Arrange MRI pituitary

# Macroprolactin result

Approximately 67 % of the prolactin immunoreactivity in this sample is due to the presence of macroprolactin. Macroprolactin is not biologically active but cross reacts in the immunoassay used to determine serum prolactin concentration. Its presence in this case makes a prolactinoma unlikely.

**Figure 4** Schematic illustrating potential sources of interference in immunometric assays for prolactin

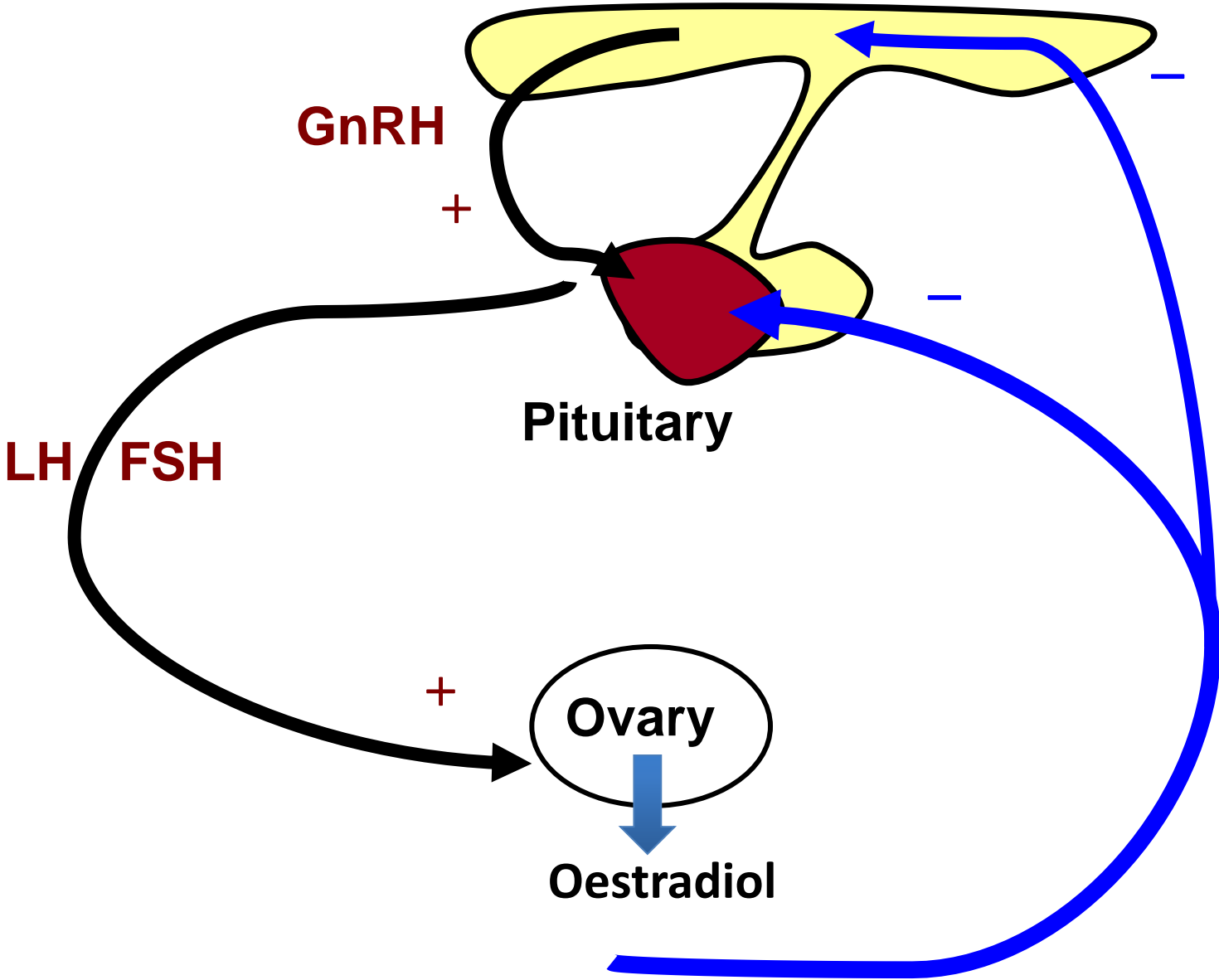


Smith TP *et al.* (2007) Technology Insight: measuring prolactin in clinical samples  
*Nat Clin Pract Endocrinol Metab* **3**: 279–289 doi:10.1038/ncpendmet0447

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# Hypothalamus



**GnRH**

+

**LH**

**FSH**

**Pituitary**

**Ovary**

**Oestradiol**

+

-

-

## Major causes of amenorrhea due to abnormalities in the hypothalamic-pituitary-ovarian axis

Abnormality	Causes
Hypothalamic dysfunction	Congenital gonadotropin-releasing hormone (GnRH) deficiency
	Functional hypothalamic amenorrhea
	- Weight loss, eating disorders
	- Exercise
	- Stress
	- Severe or prolonged illness
	- Heterozygous mutations - FGFR1, PROKR2, KAL1
	Inflammatory or infiltrative diseases
	Brain tumors - eg, craniopharyngioma
	Cranial irradiation
Traumatic brain injury	
Other syndromes - Prader-Willi, Laurence-Moon-Biedl	
Pituitary dysfunction	Hyperprolactinemia including lactotroph adenomas
	Other pituitary tumors - acromegaly, corticotroph adenomas (Cushing's disease)
	Other tumors - meningioma, germinoma, glioma
	Genetic causes of hypopituitarism
	Empty sella syndrome
	Pituitary infarct or apoplexy
Ovarian dysfunction	Polycystic ovary syndrome
	Premature ovarian failure (primary ovarian insufficiency)
	- Surgical
	- Autoimmune, genetic, ovarian toxins, idiopathic
Other	Hyperthyroidism
	Hypothyroidism
	Diabetes mellitus
	Exogenous androgen use

# Investigation of secondary amenorrhoea

Hx/Exam

Rule out pregnancy

FSH/LH/Prolactin/TSH

FSH raised

Primary ovarian  
insufficiency

FSH/LH low

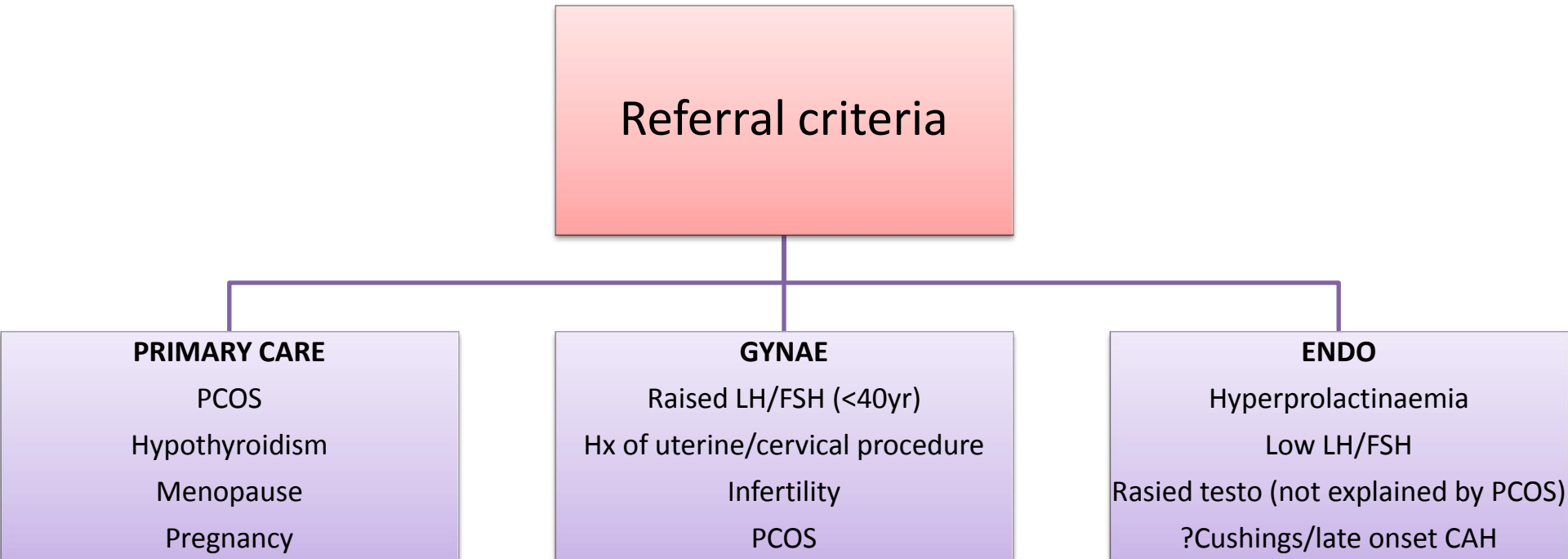
Hypogonadotrophic  
hypogonadism; rule  
out pit adenoma

Raised prolactin

Rule out pit  
adenoma



# Management of amenorrhoea – diagram adapted from NICE



# For this patient

- Dietician
- Discuss contraception
- Assess osteoporosis risk

# Take Home Messages

- Only 3-4 % of amenorrhea is due to causes other than pregnancy, lactation or menopause
- Macroprolactin is biologically inactive and can confuse diagnosis of hyperprolactinaemia
- Initial biochemical testing should include pregnancy testing, LH, FSH, TSH and prolactin.

# Case 2

32 year old female presents with secondary amenorrhoea (again!)

# Biochemical results

- Thyroid: TSH 3.31, T3 3.9, T4 <5.2
- LH 1.0, Oestradiol <70, Testosterone <0.5

# If this were your patient what would you do next?

- A. Start thyroxine and write letter for routine endocrine referral
- B. Call up lab to add on prolactin, cortisol, IGF 1 and call up the endocrine spr to discuss the case
- C. Ask the patient to come in for repeat tests in one week including FSH, TSH, prolactin, cortisol
- D. Start thyroxine and the oral contraceptive pill

# Review of all results

- Thyroid: TSH 3.31, T3 3.9, T4 <5.2
- LH 1.0, Oestradiol <70, Testosterone <0.5
- Prolactin 74
- IGF-1 6.6
- Cortisol <20 (ACTH 9.7)
- TSH and ACTH inappropriately normal

# Diagnosis

- Panhypopituitarism and secondary adrenal insufficiency due to lack of ACTH



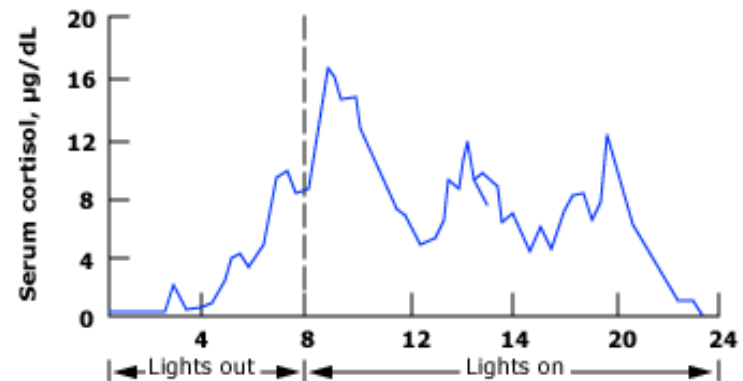
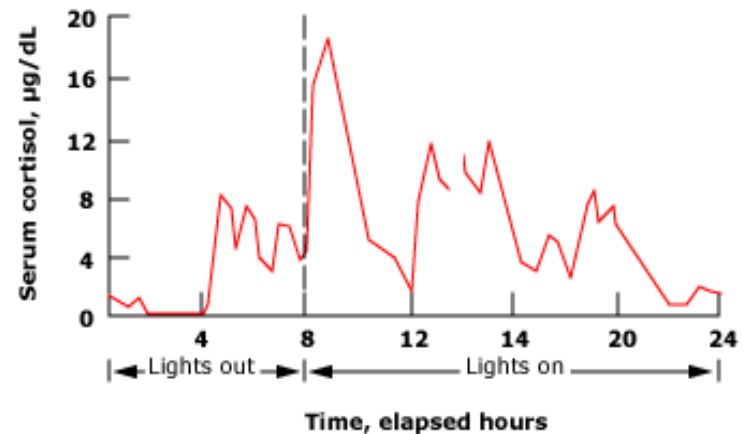
# Outcome

- Not known to have panhypopituitarism previously
- Duty biochemist called on-call team to ensure patient brought in to give urgent steroid cover that day.

# Interpretation of cortisol results

- Cortisol secretion is episodic and the normal ranges are broad.
- A single serum value, if it falls within the normal range, is inconclusive.

Circadian rhythm in serum cortisol



**You request cortisol for a 40 year old male with tiredness and mild hyponatraemia. The result from 12pm is 123 nmol/L. How do you interpret this?**

- A. This is a low value and he should be admitted for further assessment
- B. This result is from 12pm, it does not help to exclude or diagnose adrenal hypofunction

# Cortisol continued

- Patients with adrenal insufficiency have low early morning serum cortisol concentrations.
- If the value  $<80$  nmol/L, the probability of adrenal insufficiency is high.

# Other factors to consider in interpretation

- Cortisol binding globulin levels e.g. increased by oestrogens
- Hepatic and renal dysfunction
- Thyroid
- Alcohol abuse
- Depression
- Sepsis

# Defining the cause of a low cortisol

- **Clinical details** of patient including exogenous steroids
- Ensuring sample **timing**, paired ACTH more helpful
- Synacthen testing if real concern about adrenal insufficiency

# Take home messages

- Hypocortisolism has a multitude of causes
- Timing of test critical
- In the face of low T3 and T4, TSH should be raised, if inappropriately normal levels should consider secondary hypothyroidism.

# Thank you

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- [PathologyQueries@imperial.nhs.uk](mailto:PathologyQueries@imperial.nhs.uk)