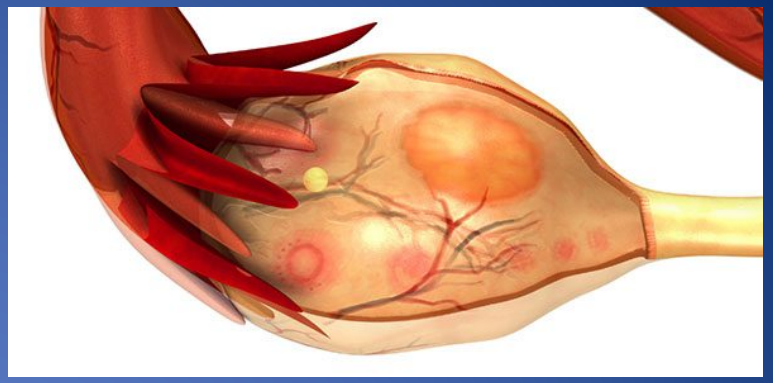
Insights into MAnaging Growth for Endocrine Nurses



Polycystic Ovary Syndrome
A case study - what happens next?

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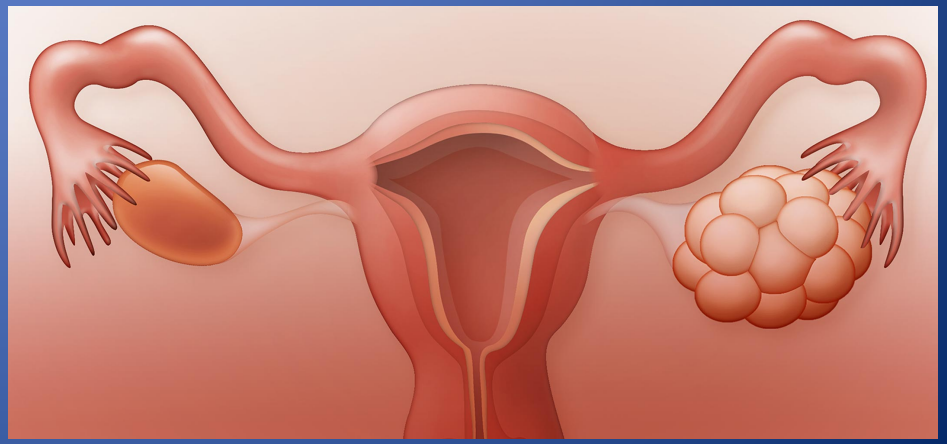
Introduction

- Case study
- Points to consider for discussion
- PCOS information
  - Diagnosis
  - Management
  - Future management



Polly

- Presented to the General Practitioner (GP) aged 13 years May 2014
  - 'High BMI'
  - Gaining weight
    - Mum 'very strict – diet and exercise'
  - Menarche – 11 years
    - Regular / heavy
    - Started on Logynon - improvement
- ? PCOS
  - Did not want an ultrasound
- No other abnormalities – endocrine cause? Referral..
- Bullying

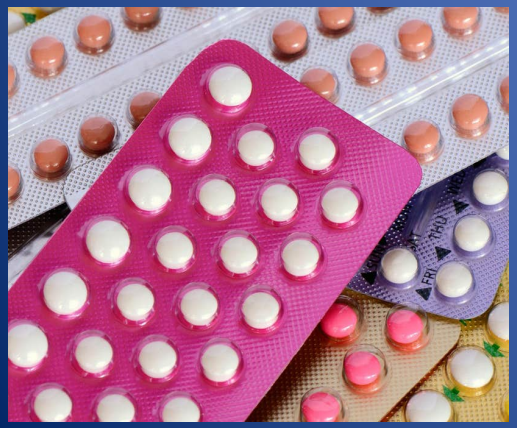
Thoughts / questions / next steps?

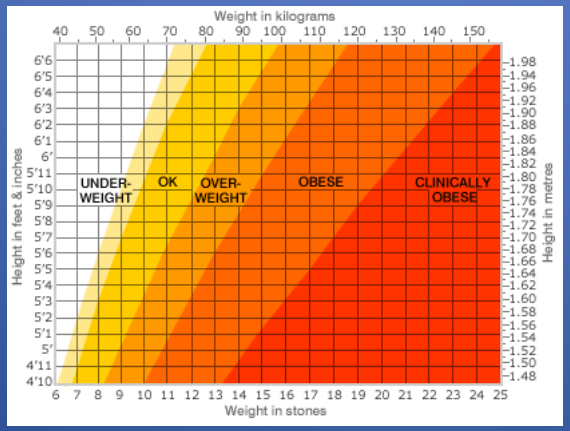
Thoughts..

- Oral contraceptive pill
  - Decreases hyperandrogenism by reducing production of androgens

    De Melo, 2017

    NHS, 2019
  - Young teenage girl..?





- Body Mass Index measurements in children
  - "Problematic in growing youth as great divergence is evident in bone, muscle, and adipose tissue development"

    Brown, 2017
    - ?Stopped growing
    - Accurate measurement ?

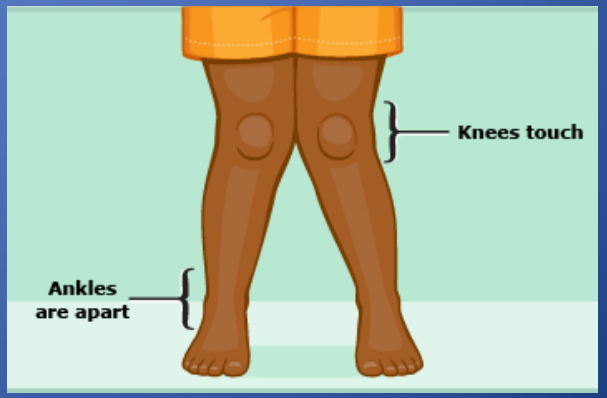
Referral to Paediatric Endocrinology July 2014

History

- Weight increasing since age 8 years
  - Parents separated
- Birth
  - 2.3kg at 41 weeks
- Second of 4 children
- Weight problems on Dad's side
  - Grandmother – 'diabetes'
- Still on OCP
  - No other medication

On examination

- Overweight
- No other clinical indications
  - Acne
  - Hirsutism
  - Acanthosis
- Genu valgum 'knock knees'



Next steps?

- Bloods
- Dietician referral
- Pelvic ultrasound

Bloods

Thyroid function tests

Vitamin D levels

Bone profile

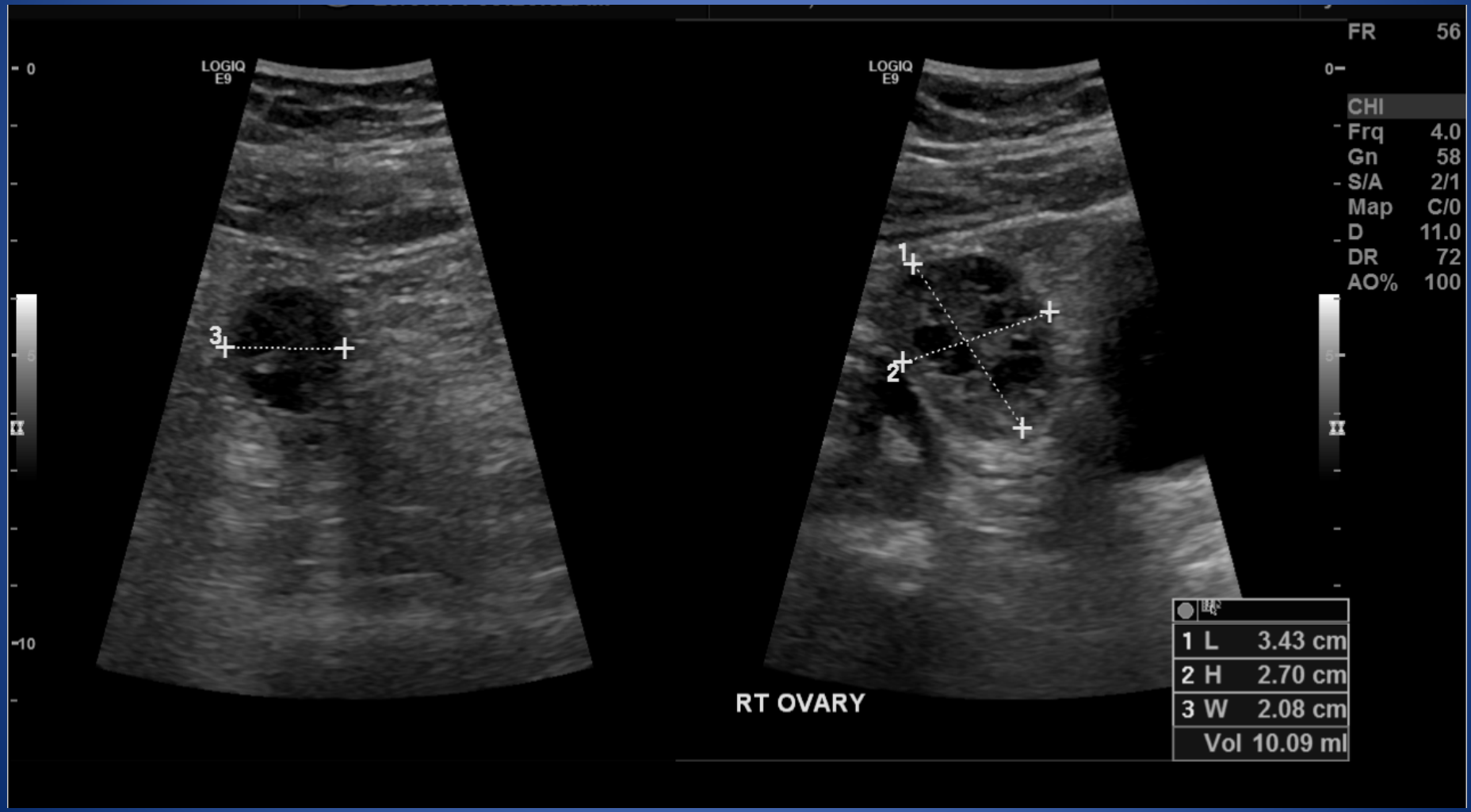
Adrenal androgens

Testosterone

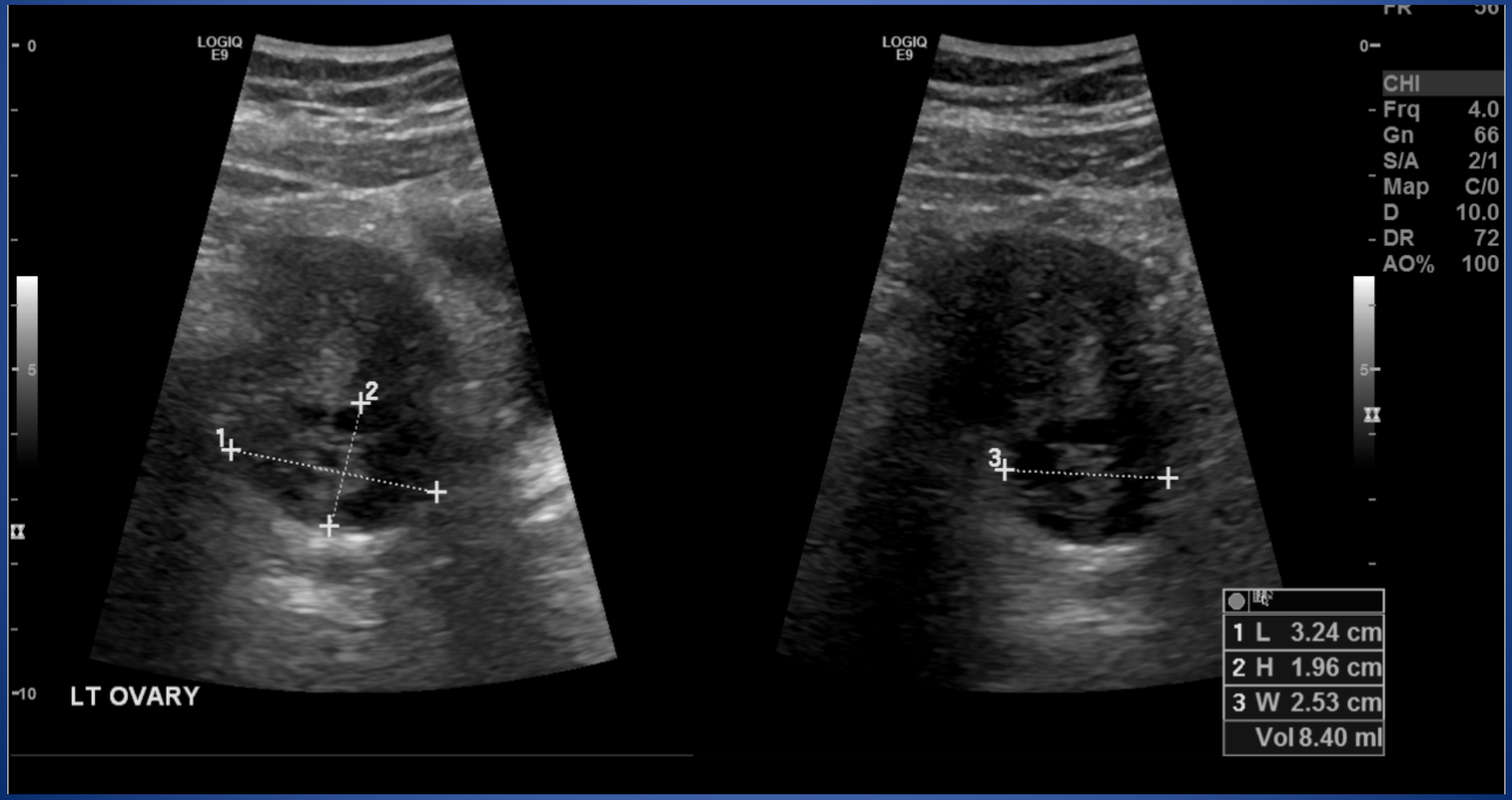
SHBG

LH / FSH

Pelvic ultrasound – right ovary



Pelvic ultrasound – left ovary

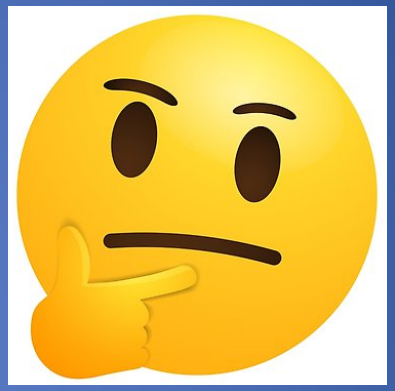


Pelvic ultrasound - report

- Both ovaries were visualized and appeared bulky with multiple microcysts, most of which were arranged around the periphery. Appearance are suggestive of polycystic ovaries
- Right ovary: 34 x 27 x 20mm
- Left ovary: 32 x 19 x 25mm
- Largest follicle is 7mm, in left ovary

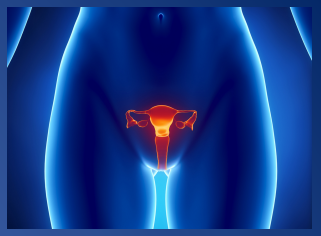
Paediatric endocrinology – March 2015

- Pelvic ultrasound reviewed
- Bloods ‘normal’
- Regular periods
  - Still heavy
  - ‘At least they are regular’
- Mum wanted no further endocrine follow up
- Referral back to GP for dietician referral..



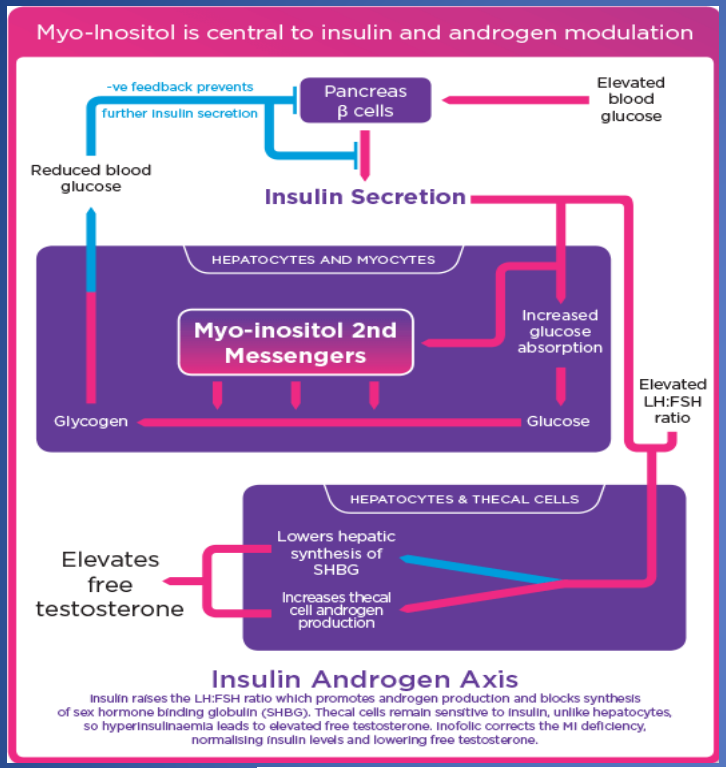
Thoughts?

Gynaecology – July 2015



- Amenorrhea since January
- Abdominal pain
- Increased BMI
- On examination
  - Abdomen soft
  - Hirsutism noted
- Investigations
  - Bloods
  - Ultrasound
- Treatment?

Inofolic sachets



- Combination of Folic Acid and Myo-Inositol (MYO)
- MYO
  - Involved in the signal of insulin from the insulin receptor, so important for patients with insulin resistance..
  - Important role in nuclear and cytoplasmic oocyte development
- Helps menstrual cycle disturbances
- Reduces obesity
- Reduces hyperandrogenism

Gynecological Endocrinology, 2012; 28(7): 509–515

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DOI: 10.3109/09513590.2011.650660

informa
healthcare

PCOS

Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials

V. Unfer[1], G. Carlomagno[1], G. Dante[2] & F. Facchinetti[2]

[1]*Gynecology Association Unfer Costabile (A.G.UN.CO.), Obstetrics and Gynecology Center, Rome, Italy and*
[2]*Mother-Infant Department, University of Modena and Reggio Emilia, Modena, Italy*

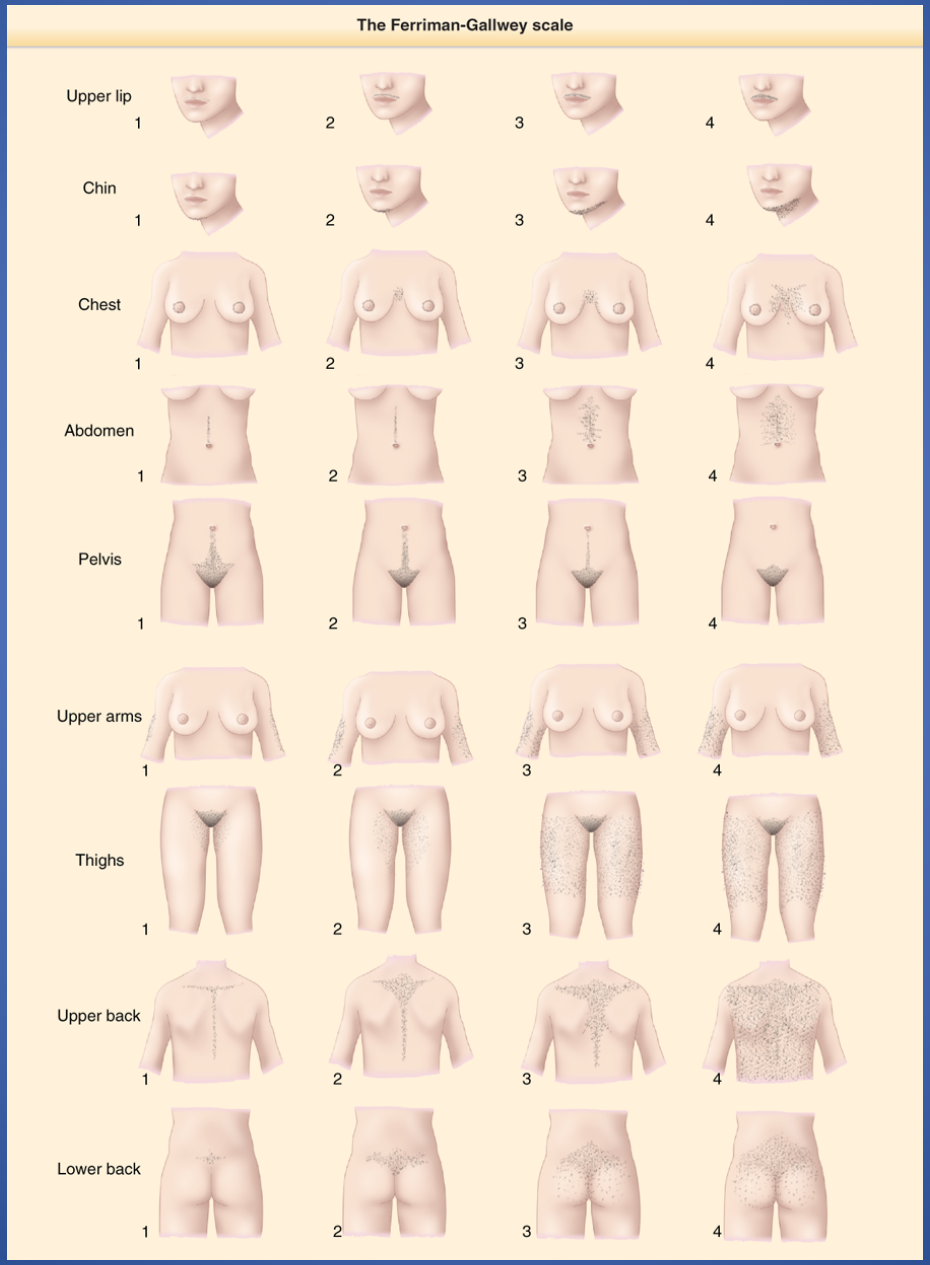
Dermatology – July 2017

- History of eczema since puberty
- Increased hirsutism
  - Face, arms, legs, back and chest
  - Waxes / hair removal creams
- 'Velvety thickened skin on neck, between the breasts and axillae'
  - Acanthosis nigricans
- Acne
- No longer on Logynon – but says has lost weight
- No mention of Inofolic sachets

Thoughts?

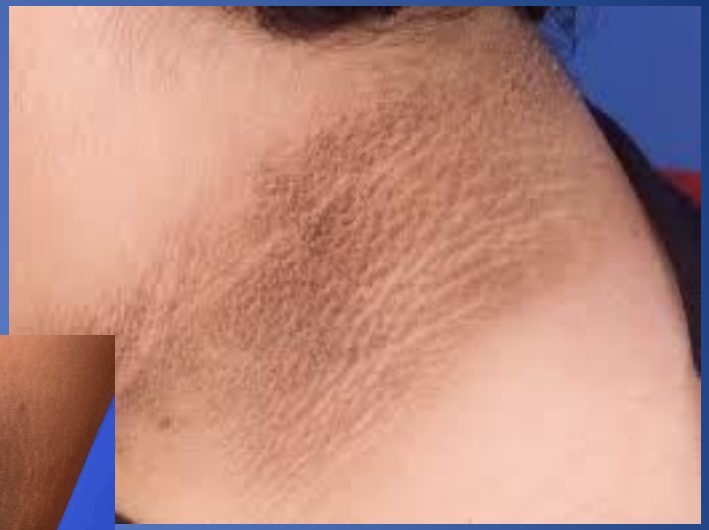
- Recommends referral to endocrinology
  - ? Insulin resistance
  - ? Metformin
- Makes referral to laser hair removal clinic

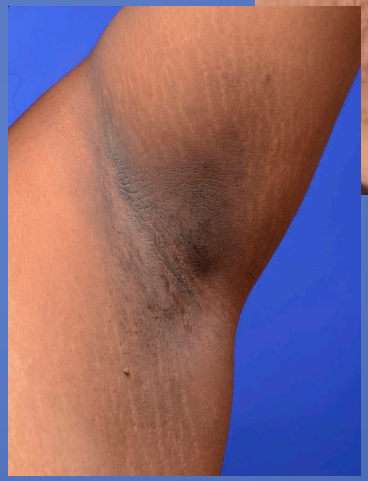
Hirsutism

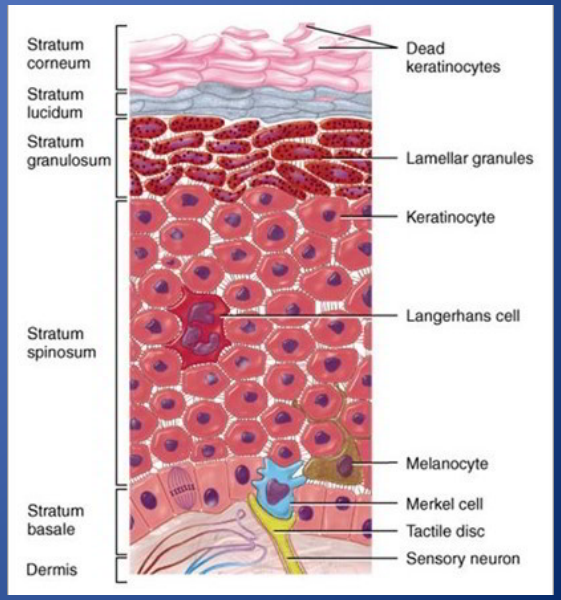

The Ferriman-Gallwey scale
Upper lip
Chin
Chest
Abdomen
Pelvis
Upper arms
Thighs
Upper back
Lower back
1
2
3
4

Acanthosis Nigricans

- Visible marker which strongly suggests Insulin Resistance
  - Higher than normal levels of insulin cause the darkened growth of skin
  - Activates keratinocyte receptors, especially IGF-1
    - Increased IGF may lead to increased keratinocyte and dermal fibroblasts

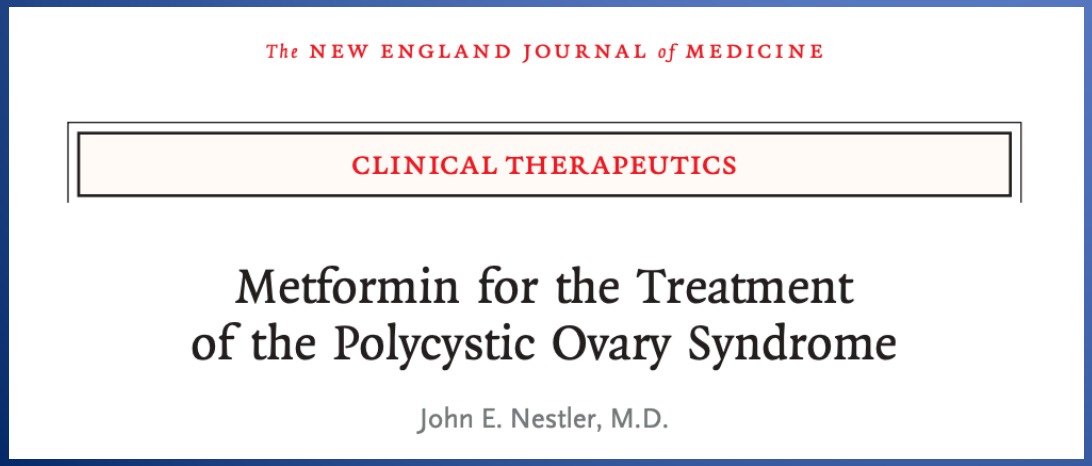


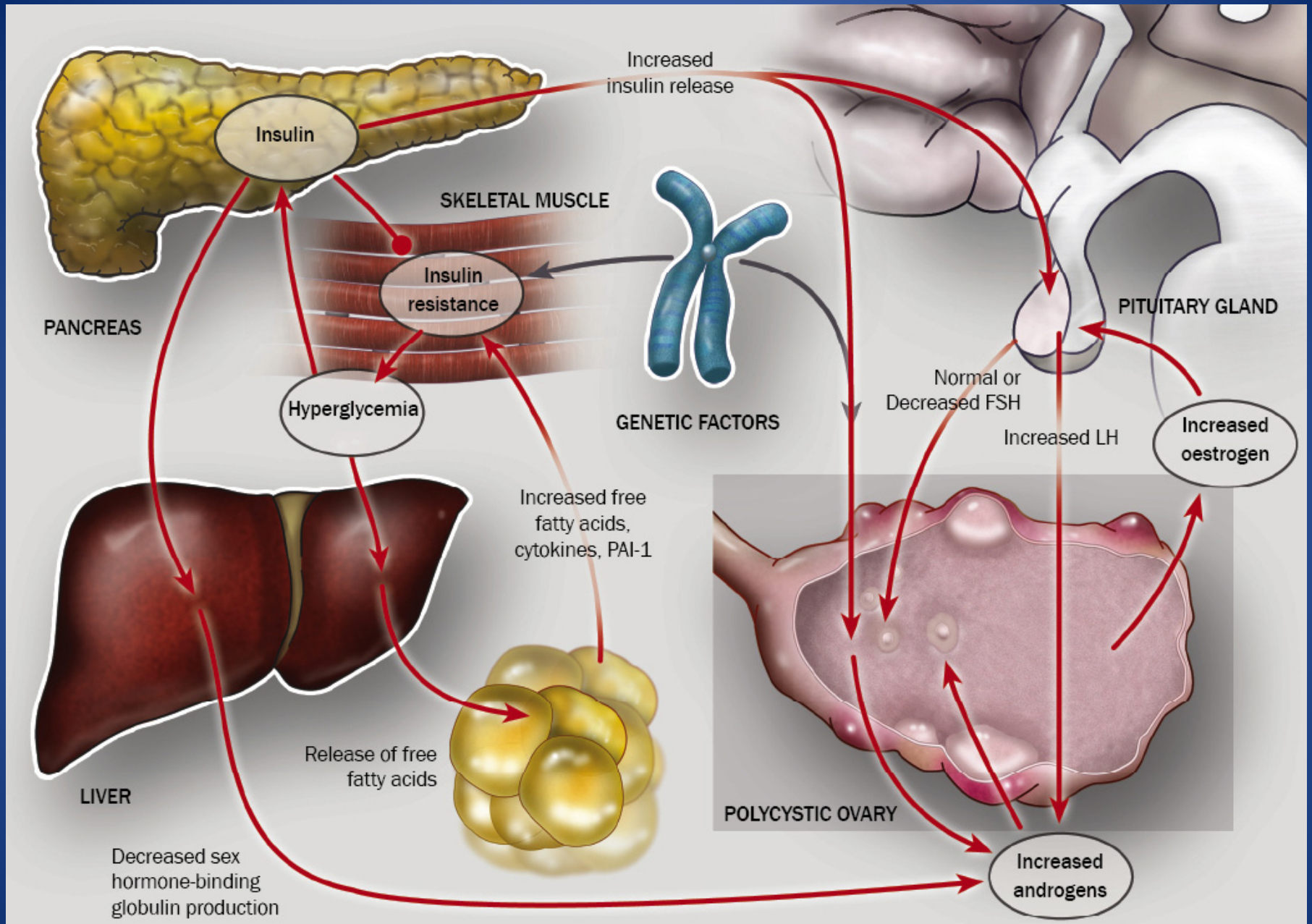




Metformin

- Used widely to treat Type 2 diabetes
- Increase in insulin action at an intracellular locus
  - Results in decreased hepatic glucose production
- Stimulates tissue uptake of glucose
- Reduces gastro-intestinal absorption of carbohydrate
  - Does not cause hypoglycaemia
  - Not associated with weight gain

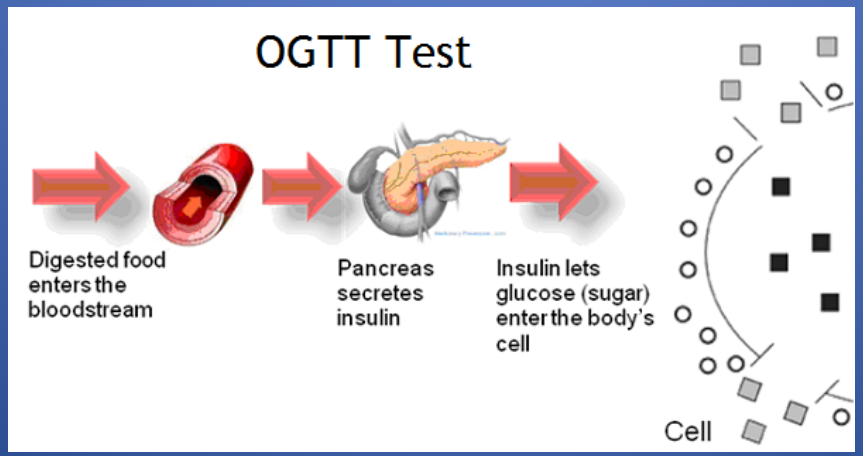




Adapted from Nestler J E, et al. New England Journal of Medicine 2008; 358: 47-54

Paediatric Endocrinology – January 2018

- Oral Glucose Tolerance Test
  - Used to measure how the body can process large amounts of sugar
  - Oral glucose solution
    - 1.75g/kg, up to 75g
  - Baseline, 120 minutes
    - Glucose
    - Insulin
  - Fasting baseline glucose should be below 6.1mmol/L
  - Between 6.1 and 7.0 is borderline
  - 120 minute sample, glucose is normal if below 10mmol/L



Paediatric Endocrinology – July 2018

Age 17 years

	0	120
Glucose	4.5mmol/L	5.5
Insulin	44miu/L	310

- Androstenedione ↑ 9.3 nmol/L (2-5.4)
- DHEAS N 4.4umol/L (1.6-7.8)
- SHBG ↓ 14nmol/L (20-130 females)
- Testosterone 2.1nmol/L (0.2-2.9)
- Liver Function, Fasting Lipids
- HbA1c 24mmol/mol (20-41)

- Periods now regular
- 'Exercises loads'
- Due laser treatment for hirsutism

Thoughts?

DIET

- Skips breakfast
- Snacks on crisps
- Drinks LOTS of juice

general contour of the breast.

elsewhere above the base of the inverse triangle ... and rated stage 6)

Girls Height

cm / in

50th centile maturity cohort: 97, 50, 3

Early (90th centile) maturers: 97
Early (90th centile) maturers: 50
Late (10th centile) maturers: 50
Late (10th centile) maturers: 3

97 90 75 50 25 10 3

Adult target range: To calculate the range of adult heights expected for girls of these parents, plot the Mother's height and then the Father's height **minus** 13cm on the right hand vertical scale. Calculate the midpoint between these and then, for every 5cm this point diviates from the population 50th centile, go 1cm nearer to that centile. Plot the resulting point X. The girls height should be within a range of ±9cm of X.

Father's Height cm

Mother's Height cm

Breast stage: 5+ 4+ 3+ 2+ — 97 90 75 50 25 10 3

Pubic hair stage: 5+ 4+ 3+ 2+ — 97 90 75 50 25 10 3

Menarche — 97 90 75 50 25 10 3

Peak height velocity — 90 50 3

Age, years

Reg. No.

Surname

Forename

Date of Birth / / .

Decimal Yr.

Notes/Treatment

Girls Weight

kg / lb

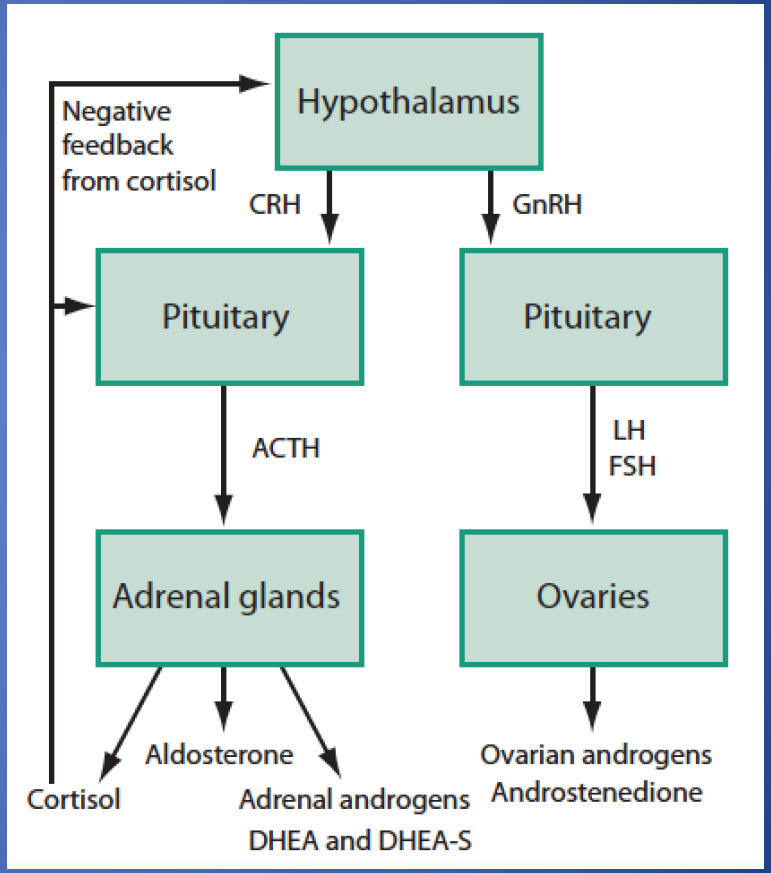
Centiles: 97, 50, 3

97 90 75 50 25 10 3

Age, years

Role of Adrenal Androgens

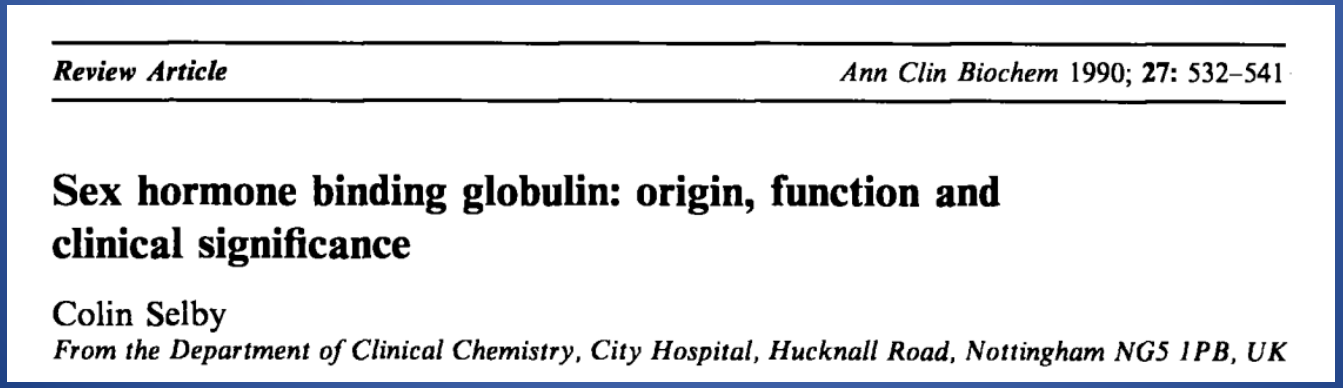
- DHEA is the predominant androgen
  - DHEAS
- Ovary
  - 20% of DHEA
  - 50% of Androstenedione
  - 25% of circulating Testosterone
- Healthy women
  - 80% of circulating Testosterone is bound to SHBG
- PCOS
  - Increased Testosterone
  - Elevated DHEAS
  - Lower SHBG



Meek et al (2013) The Obstetrician & Gynaecologist

Sex Hormone Binding Globulin

- Made in the liver
- Usually twice as high in women than in men
- Lower levels in PCOS, because of the androgens and oestrogens
- Decreases with high insulin levels
- Obese girls likely to have an earlier menarche due to the lower SHBG levels



Review Article *Ann Clin Biochem* 1990; **27**: 532–541

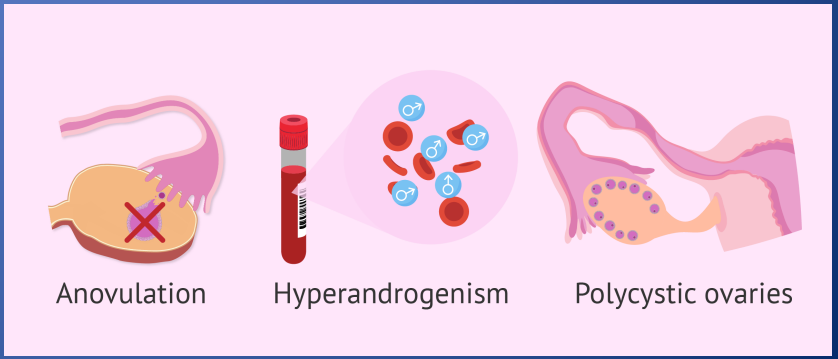
Sex hormone binding globulin: origin, function and clinical significance

Colin Selby

From the Department of Clinical Chemistry, City Hospital, Hucknall Road, Nottingham NG5 1PB, UK

What is PCOS?

- 8 – 13 % of all women
- Increased prevalence as BMI increases
- 2 of the 3 Rotterdam criteria are required for diagnosis
  - Polycystic ovaries
    - 12 or more follicles measuring 2-9mm in diameter, or increased ovarian volume
  - Oligomenorrhoea / anovulation
    - Reduced periods / failure to release eggs)
  - Hyperandrogenism
    - Clinically
    - Biochemically



What causes it?

- Strong family history
  - Genetics?
  - Studies still in their infancy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Polycystic ovary syndrome: Scientists closer to understanding cause

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Best Practice & Research Clinical Obstetrics and Gynaecology 37 (2016) 56–65

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Best Practice & Research Clinical Obstetrics and Gynaecology

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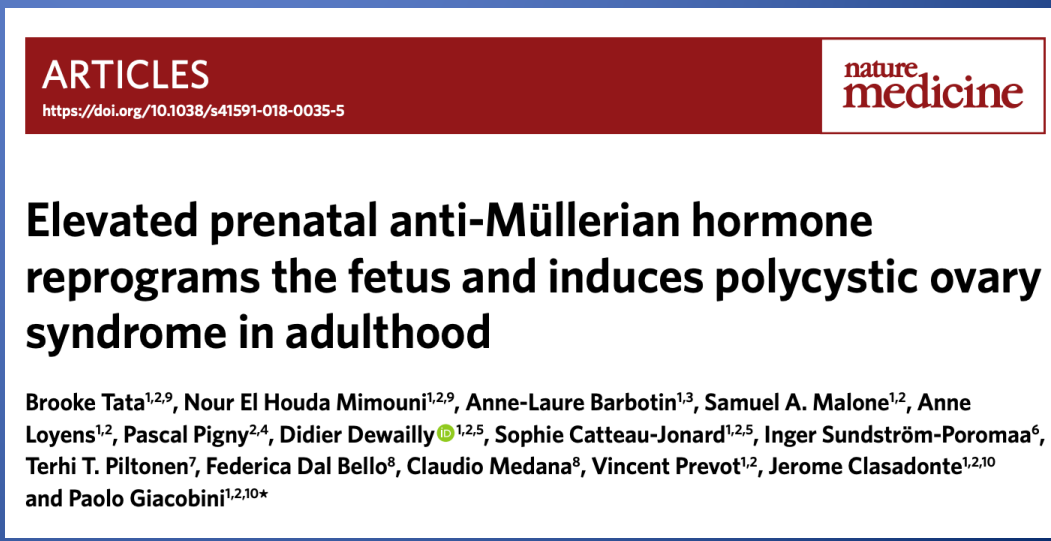
6

Genetic Studies on Polycystic Ovary Syndrome

Han Zhao, PhD, MD [a, b, c], Yue Lv, PhD [a, b, c], Lei Li, PhD [a, b, c], Zi-Jiang Chen, PhD, MD [a, b, c, d, e, *]


ARTICLES

https://doi.org/10.1038/s41591-018-0035-5

nature medicine

Elevated prenatal anti-Müllerian hormone reprograms the fetus and induces polycystic ovary syndrome in adulthood

Brooke Tata[1,2,9], Nour El Houda Mimouni[1,2,9], Anne-Laure Barbotin[1,3], Samuel A. Malone[1,2], Anne Loyens[1,2], Pascal Pigny[2,4], Didier Dewailly[1,2,5], Sophie Catteau-Jonard[1,2,5], Inger Sundström-Poromaa[6], Terhi T. Piltonen[7], Federica Dal Bello[8], Claudio Medana[8], Vincent Prevot[1,2], Jerome Clasadonte[1,2,10] and Paolo Giacobini[1,2,10]*

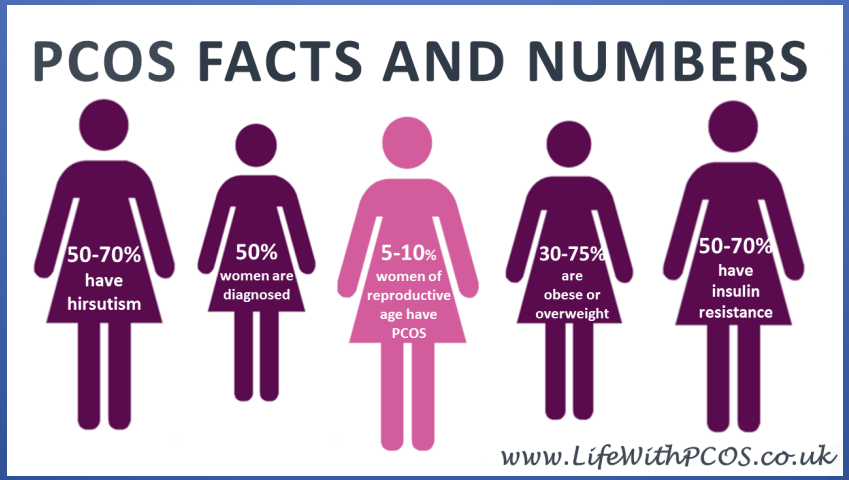
Management – multidisciplinary approach

- Hyperandrogenism
- Metabolic
  - ↑risk of cardiovascular disease, T2D, abnormal lipids, obstructive sleep apnoea
- Reproductive -
  - Oral contraceptive pill
    - Reduce ovarian androgen production by suppressing GnRH
    - Oestrogens increase the SHBG levels
- Psychological
  - ↑ depression
  - Anxiety
  - Psychosexual dysfunction
  - Disordered eating
  - Feminine identity challenged
- Cognitive behavioural therapy, psychotherapy, support groups

Where next for Polly?

- No Metformin
- Discharge back to the General Practitioner, but keep under review
- Refer to adult obesity clinic in 6 months

Thoughts?



Conclusion

- PCOS management – complex
- Education
- Support