

To refer or not to refer?
That is the question!

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DISCLOSURE

- No conflicts of interest

Objectives

- To recognize what common pediatric endocrinology questions do **not** need referral, and how to manage them
- To put together all the information required prior to a pediatric endocrinology referral
- To highlight the cases and/or red flags that require urgent referral to pediatric endocrinology

Case 1

- A 21 month old baby with suboptimal growth
- What growth parameter is affected?
- Is it primarily weight?
- GROWTH CURVES

Special Considerations for 0-24 months

- Birth/perinatal history
- It is the one time of life where you are ALLOWED to cross percentiles!
- Birth parameters are a reflection of intrauterine environment
- It is only after that our own growth potential kicks in
- Measurement accuracy

Red flags

- Neonatal hypoglycemia
- Microphallus in a boy
- Midline defects
- Any evidence of pituitary deficiencies

Case 2

- 10 year old boy
- Referred for short stature
- The key: growth velocity
- Familial vs constitutional delay
- Familial: heights of parents → measure them!
- Constitutional: delayed puberty, drift off in first 18-24 months, delayed dentition, + familial history

What do we need?

- Send us the growth curve!
- Accurate measurements
- Mid-parental height

If the growth velocity is poor...

- <2 cm/6 months
- Start with a baseline work-up
- CBC, CRP, lytes, total protein, albumin, TTG/IgA, TFTs, AST/ALT, BUN/creatinine, IGF-1
- Bone age X-ray → left hand and wrist
- Do not bother with a random growth hormone level
- Please refer sooner rather than later

Case 3

- 5 year old girl
- Petite for her age
- The key: growth velocity

Special considerations

- Think about Turner syndrome
 - Classic dysmorphic features (not always present)
 - Isolated SS
 - In keeping with genetic potential?
 - Recurrent OM/language delay
 - School difficulty
 - Strabismus

What do we need?

- Growth curve
- Send us the basic work-up
- Consider a microarray
- Girls with Turner syndrome **do** qualify for GH Rx

Difficult cases

- ISS/SGA → not routinely covered in Quebec
- Treated in another country... does NOT mean they qualify in Canada
- Prader-Willi syndrome → not black and white

Case 4

- 9 year old girl who is petite who has started puberty
- Is this precocious?
- Can we stop it?

Definitions of precocious puberty

- **Onset** of secondary sexual characteristics < 7 yo F or < 9 yo M
- True central puberty:
 - Thelarche in a girl
 - Testicular enlargement in a boy
- Refer immediately
- If you refer late Rx becomes controversial → do not promise Rx
- Rx goals
 - Preserve final adult height
 - Psychological

Special considerations

- Referring children with normal puberty
- Rx with LHRH agonist may interfere with the natural growth spurt

Benign variants

- Benign premature thelarche
 - Onset generally < 2 yo
 - Isolated
- Benign premature adrenarche
 - Pubic hair or axillary hair or body odour or acne
 - No other signs of true central puberty
 - Dx of exclusion
 - Baseline work-up → total testosterone, DHEAS, 17-OHP
 - +/- bone age Xray

Going back to our 9 yo girl

- Expectations?
- Menarche may be normal at age 9
- When was the onset?
- Even if it was precocious, it may be too late, but still important to identify pathology (more common in boys vs girls for true central puberty)
- There will usually still be growth after menarche

Case 5

- 16 year old F with a growth plateau
- When is it normal to plateau?
- Know when puberty began and how it progressed
- A plateau is normal upon completion of growth
- Consider a bone age Xray prior to referral → this can help temper expectations

Red flags

- Lack of a pubertal growth spurt, ever, despite going through puberty
- Plateauing before completion of puberty
- The key is the curve
- Even if done growth, these patients should be referred in order to identify pathology even if it is too late to treat for growth
- Deficiency in 1 pituitary hormone imparts a lifelong risk of developing other pituitary deficiencies (TSH, ACTH, LH, FSH, ADH)

Case 6

- A 9 year old boy has blood work done and is found to have a TSH of 6.89 mIU/L and a normal free T4
- Does this warrant immediate referral?

Key questions

- Family history?
- Goiter on exam
- When the TSH was drawn, was she unwell in any way?
- Symptoms of hypothyroidism: Fatigue, suboptimal growth, weight gain, cold intolerance, constipation, dry skin → less relevant in this case because a TSH < 10 should NOT cause significant symptoms

Next step?

- Reassure the family that this is simply a borderline result that needs to be followed
- Repeat it in 1-2 months with anti-TPO antibodies
- If the TSH is rising or > 10 consider Rx
- If TSH > 20 → should be seen quite quickly by endo

- BUT you can start Rx before referral
- Repeat TSH 6-8 weeks after Rx initiation or any dose change

Case 7

- An 11 year old girl is found to have +anti TPO antibodies
- Done in the context of a positive family history of hypothyroidism
- Normal TFTs

- What does this mean?

- What if she has a goiter?

Case 8

- A 13 year old girl has had a decline in school performance and teachers are concerned about possible ADHD
- TSH found to be <0.02 with a free T4 of 36 pmol/L (normal 8-18)

- Hyperthyroidism!
- Graves
- Hashitoxicosis
- Subacute thyroiditis

Next steps?

- Palpitations, difficulty with sleep, heat intolerance, weight loss
- Proper clinical assessment with BP and HR
- IMMEDIATE referral to endo
- Consider initiation of a beta blocker
- Methimazole → risk of agranulocytosis (fever and sore throat)

Case 9

- An asymptomatic 15 year old boy has routine bloodwork done
- TSH is found to be low at 0.1 with a normal free T4
- What do we make of this?

Diagnostic possibilities

- Hyperthyroidism with a high T3
 - Hashitoxicosis → starts off hyper and becomes hypo
 - Subacute thyroiditis in recovery
 - Sick euthyroid syndrome
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- What do we NOT want to miss?

Central hypothyroidism

- Low TSH with a normal or low free T4
- Low free T4 with an inappropriately normal TSH
- Less symptomatic than primary hypothyroidism
- BUT MUCH MORE WORRISOME

Next steps?

- Full clinical assessment keeping in mind the possibility of central hypothyroidism (neuro symptoms, visual fields)
- Growth curve and puberty
- Repeat TSH as soon as possible with a free T4, free T3, anti TPO and anti TSH receptor antibodies

- Do a morning cortisol
- Consider a pituitary profile → or leave that to us!

Case 10

- A 3 year old boy has polyuria and polydipsia
- RULE OUT DIABETES

Next steps?

- Urinalysis in the office → immediate result
- If you have access to a lab, have the urinalysis done immediately and follow up on the result IMMEDIATELY
- Difficult lab access → send them straight to the ER

- Do not bother with an A1C, fasting blood work etc

- TIME IS OF THE ESSENCE
- Let endo know you are sending the patient in

Case 11

- A 15 year old girl is referred to you for secondary amenorrhea
- Her first period was at the age of 10, she had irregular periods for the first year followed by regular periods
- Stopped having periods 8 months ago

- What do we do now?

Key questions

- Central symptoms – headaches, visual changes (including peripheral vision), galactorrhea
- Signs of estrogenization – vaginal discharge, breast tissue
- Hirsutism, acne, family history of PCOS

- Stressors or life changes – weight, nutrition, activity

Functional HH with an eating disorder

- Common
 - Ask the right questions
 - Send to Adolescent Medicine, not Endo
 - Recovery from the eating disorder is key
 - Resumption of menses may take a while...
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- On the way to recovery → rising estradiol, vaginal discharge

Next steps?

- Full history and exam (neuro exam, visual fields), Tanner staging
- Growth curve
- Basic work-up: bhCG, LH, FSH, E2, prolactin, TSH, testo, DHEAS, 17-OHP
- If worried about something central → add an am cortisol and free T4

- No need for an ultrasound if secondary
- Leave the rest to us!

Case 12

- An 11 year boy with significant weight gain
- Parents are very concerned

Proper history

- Detailed nutritional history: meals, snacks, quantities, types, beverages
- Activity history
- Screen time

- The key is in the CURVE

- If they are growing well in terms of height, it is NOT ENDOCRINE
- Most obesity is EXOGENOUS

Endo causes?

- Cushing's
- Hypothyroidism
- GH deficiency

- Unifying feature is POOR GROWTH

Next steps?

- Cushing's → HTN, thick violaceous striae, proximal muscle weakness, supraclavicular fat
- If you are truly suspicious, you can do a dex suppression test
- Dex 1 mg at 11 pm followed by an 8 am cortisol

- Hypothyroidism → easy to do a TSH

What will endo do?

- NOT VERY MUCH
- No magic pill or interdisciplinary team
- Clinique 180, Circuit
- Nutritionists within the hospital will not see patients with obesity only
- CLSS versus private nutritionist

Other considerations?

- COMORBIDITIES
- OSA → Resp
- Fatty liver → GI
- Glucose intolerance or dyslipidemia → consider endo

- Normal BG and high insulin → healthy active living
- No medical Rx unless LDL \geq 4.2 → the rest is healthy active living

- Severe obesity clinic with the possibility of gastric bypass surgery

PEARLS

- Many endo findings may not warrant immediate referral → consider discussing with endo, starting the next steps and **then** see if endo is actually needed
- We are often there to **reassure** the family that there is no endocrinopathy
- Realistic expectations
- Urgent referrals: new onset T1DM, hyperthyroidism, central pituitary issues
- Attach a growth curve and all results

Where to refer?

- Send to only one:
 - MCH (TCC, Brunswick, Angus)
 - Ste Justine
 - Agoo
- All centres triage referrals!
- If you are really worried, call peds endo on call!