# DIFFUSE HAIR LOSS IN CHILDREN AND ADOLESCENTS

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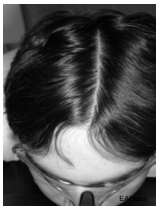
## TELOGEN EFFLUVIUM

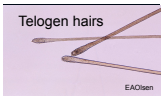
Physical exam:

- Global decrease in hair density
  - Confirm by performing midline part in back and top of scalp —should be similar
- Preservation of follicular ostia on scalp and scalp is generally normal



## Hair Loss Evaluation in Telogen Effluvium: Hair Pull

- Grasp a small clump of hair at the roots and gently pull through to the ends. Be very gentle with this in young children.
- Repeat in representative areas of entire scalp including occiput. Hair pull in TE should be positive in all areas. 3-4 hairs/ pull is abnormal.
- Perform microscopic hair exam of proximal ends of hairs
  - All hairs in an adolescent with TE should be telogen hairs--any anagen hairs are abnormal
  - In children less than 5 years, one can artificially induce "loose anagen" like hairs on too firm hair pull which can confuse picture





## Etiology of Telogen Effluvium

- Look for causes that occurred 3-6 months prior to onset
  - Stress
  - Medical or surgical event especially thyroid related
  - Medications
  - Nutritional
    - Protein (kwashiokor)
    - Calories (maramus)
    - Vitamins
      - Biotin
      - Zinc
      - Iron

## Telogen Effluvium and Medications

- Any medication can cause TE but ones of particular concern in children/adolescents
  - Isotretinoin
  - Vitamin A doses of >15,000 IU
  - Lithium (evaluate for lithium hypothyroidism)
  - Sodium valproate—alters zinc and selenium homeostasis and causes hyperandrogenism so may also promote AGA
  - Amphetamine for weight loss
  - Medications for ADHD
  - Antidepressants

## Biotin Deficiency

- Relationship to hair loss raised because of the biotin responsive hair loss associated with hereditary forms of biotin deficiency (holocarboxylase and biotinidase)
- Acquired forms of biotin deficiency
  - Parental alimentation
  - Egg white diet
  - Gastric disease
  - IBD
  - Chronic hemodialysis
  - Medications: Lipoic acid, certain anticonvulsants (carbamazepine, phenobarbital, phenytoin)

## Biotin Deficiency

Clinical Picture:

•Full blown: infancy; neurological defects, dermatitis especially periorificial, keratoconjunctivitis, hair loss

•Partial: later childhood, less severe symptoms-- seborrhea or eczema, depression, lethargy, paresthesias, thin hair +/- loss of hair color

Diagnosis:

•Biotin level, +/-ketoacidosis and lactic acidosis, organic acidosis

•Biotinidase <5% in severe, 15-30% NL in partial

Treatment: Biotin 10 mg/day. Oral and topical EFA noted to help

## Zinc Deficiency

- Hereditary: AR, abnormal gene SLC39A4 on Chromosome 824.3 which encodes Zip 4 transporter important in GI absorption
- Acquired
  - Abnormal absorption
    - Pancreatitis
    - Intestinal bypass or short bowel syndrome
    - Crohn's disease or ulcerative colitis
    - Celiac disease
    - Diet high in phytates (refined cereals), fiber
  - Certain drugs: sodium valproate, penicillamine, diuretics
  - Inadequate diet
  - Increased urinary excretion related to alcohol
  - Chronic renal disease
  - Sickle cell disease
  - Liver disease

## Acquired Zinc Deficiency

Clinical findings

•Poor appetite

•Mild growth retardation

•Hypogonadism (low T)

•"Rough" skin

•Mental lethargy

•Taste abnormality

•Impaired wound healing

•Increased susceptibility to infections

•Hair loss

Diagnosis: Serum zinc <70 ug/dL. Have drawn fasting and off of supplements containing zinc

## Zinc Deficiency

- Treatment:
  - Supplemental zinc: 0.5-1 mg/kg/day x up to 6 months. UL tolerated dose=40 mg/day
  - Monitor both zinc, copper/ceruloplasm and iron levels as zinc will depress copper absorption through induction metallothionein and can lead to a non-iron responsive microcytic anemia and neutropenia and also impair iron absorption
- Maintenance zinc:
  - 1-10 years: 10 mg/day
  - >10 years: 15 mg/day
- Potential for high zinc levels: Zinc lozenges for colds: doses range from 5-14 mg per

## Iron Deficiency (ID) and Hair Loss

- Many publications have linked either low levels of iron or lower ferritin levels in hair loss patients compared to controls
  - Difficulties in proving the interrelatedness of ID and hair loss have included:
    - Definition of ID is not uniform across all previous studies (ferritin <10 ug/L to <70 ug/L used)
    - Many publications without control population
    - Control populations have been drawn from varied populations, of small numbers (largest =46 subjects prior to Duke study of 96) and not necessarily screened for hair loss
- Many articles disputing relationship of hair loss and ID
  - No well controlled trials showing whether treatment of ID affects hair growth

## Identification of Iron Deficiency

- Most studies use serum ferritin which is an excellent indicator of iron stores in healthy patients as only iron deficiency causes low serum ferritin
- Acute phase reactant with elevation in the face of inflammation
- Serum levels used to identify ID:
  - <10-15 ng/mL: sensitivity 75%, specificity 98%
  - <40 ng/mL has sensitivity 98%, specificity 98%
  - <70 ng/mL is reasonable level to define ID in patients with underlying inflammatory disease.

  >70 ng/mL is the benchmark for assuring adequate BM iron stores

## Iron Deficiency in Children and Adolescents

- Risk Factors
  - Rapid body growth
  - Heavy menses
  - Pregnancy
  - GI bleeding: Aspirin, NSAID (1 ml blood=0.5 mg iron)
  - Inadequate diet
  - Erythrodermic skin conditions
  - Poor absorption—celiac disease one cause
  - Genetic deficiency of key iron enzyme. Note ferritin is an unreliable indicator of these conditions

## Duke Study on Iron Deficiency in FPHL, CTE and Controls*

- All subjects were Caucasian women who had not been pregnant in the past year and on no anticoagulants
- Controls
  - Selected from volunteers who were screened for normal hair growth, good health, and who had serum ferritin, ESR and hemoglobin obtained in absence of iron supplementation
- Hair loss subjects:
  - Olsen Hair Disorders Database utilized to identify those with established diagnosis of FPHL or CTE who had a serum ferritin and hemoglobin
  - History on iron supplementation at time of blood draw unknown and no ESR available majority

*Olsen EA, Reed KB, Cacchio PC, Caudill L: Iron deficiency in female pattern hair loss, chronic telogen effluvium, and control groups. J Am Acad Dermatol. 63(6):991-9, 2010.

## Results of Duke Iron Deficiency Study

| Group | Number subjects | Serum Ferritin Levels | | |
|---|---|---|---|---|
| | | ≤ 15 µg/L | ≤ 40 µg/L | ≤ 70 µg/L |
| Controls | N=76) | 21.1% | 52.6% | 81.6% |
| CTE | N=121 | 11.5% | 53.1% | 75.0% |
| FPHL | N=285 | 7.7% | 45.6% | 75.4% |

Olsen EA, Reed KB, Cacchio PC, Caudill L: Iron deficiency in female pattern hair loss, chronic telogen effluvium, and control groups. J Am Acad Dermatol. 63(6):991-9, 2010.

## Treatment of Iron Deficiency

- Increase heme iron in diet (meat, poultry, fish—2-3x absorption over iron-fortified or foods with non-heme iron
- Absorption of iron supplements varies with type of iron:
  - 20% ferrous sulfate. 325 mg of ferrous sulfate delivers about 60 mg of elemental iron.
  - 12% ferrous gluconate
  - 33% ferrous fumerate.

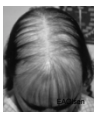
## Treatment of Iron Deficiency

- Divide total dose into multiple doses on an empty stomach and start with ferrous sulfate (GI irritation/absorption best)
- Absorption increased in mildly acidic medium—Vitamin C, no food
- Absorption decreased with: antacids, proton pump inhibitors, levothyroxine, levodopa, cholestyramine, calcium and certain foods [soy products, tannates (tea)]
- Treatment should try to replace to normal levels ie in healthy subject to serum ferritin 40 ug/L

## Screening Labs for Telogen Effluvium

- Ideally do all tests off of any vitamin supplements for at least 24 hours
- CBC with diff
- TSH and free T4
- Ferritin
- Iron/TIBC (% transferrin sat) or ESR as further screen for potential inflammation skewing ferritin
- If severe dietary issues, consider a fasting zinc and biotin level

## Diffuse Alopecia Areata



Alopecia areata may present with diffuse loss that can mimic telogen effluvium or severe FPHL

Estimated incidence <3% of children (Katsarou A. JAAD 2014)

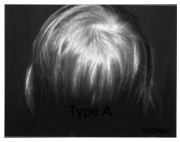
Key features are the positive hair pull for dystrophic anagen hairs and presence of "exclamation point" hairs on physical exam

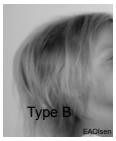
Yellow dots common on dermoscopy

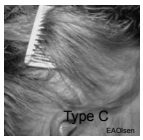
Look for nail abnormalies and hair loss on body, eyebrows or eyelashes

Biopsy may only show miniaturization

## Loose Anagen Syndrome*



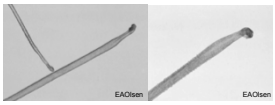




- Diffuse thinning
- Short and very slow-growing
- +/- change in hair texture

-Onset usually < 8 y. o.

-+ Hair pull for primarily LA

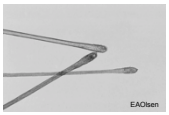
- hairs, some telogen hairs



*Olsen EA, Bettencourt MS, Cote N: The presence of loose anagen hairs obtained by hair pull in the normal population. J Investig Dermatol Symp Proc (suppl) 4:258-260, 1999.

## Short Anagen Syndrome*

- Young children
- Presents as decreased density, increased shedding and inability to grow hair long
- Etiology is short anagen phase
- Hair pull is key:
  - Proximal ends: may be increased but only telogen hairs
  - Distal ends (if no hair cut): tapered ends



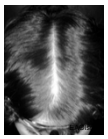
*Antaya RJ, Sideridou E, Olsen EA.: Short anagen syndrome. JAAD, 53: S130-S134, 2005.

## Androgenetic Alopecia in Adolescents

- Clinical Clues
  - Both girls and boys: widened part may be only sign
  - Absolute sparing occiput
  - Bitemporal recession
  - Hair pull: negative except in affected areas and telogen hairs only
  - Variability in hair diameter central>occipital scalp
  - +/- perifollicular pigmentation on dermoscopy

## Androgenetic Alopecia in Adolescents

- These children are more likely to have the following:
  - More rapidly progressive course and higher pattern of loss
  - In girls, more likely to have hyperandrogenemia related symptoms, PCOS and insulin resistance—check for hirsutism, acanthosis nigricans
  - At risk for metabolic syndrome



## Scalp Biopsy: Utility

- Diagnosis:
  - Acute alopecia areata
  - Presence of scarring and follicular loss
  - Trichotillomania
  - Infection
  - Tumor
  - CTD
- What it can only suggest:
  - Telogen effluvium
  - Androgenetic alopecia/Pattern hair loss
  - Long standing alopecia areata

## Scalp Biopsy

4 mm, horizontal sections always best

No. of follicles—number at birth is number for life

•Normal Child: no standard in 4 mm but higher than adult (smaller head)

•Normal adult Caucasian: ~36

•Normal adult African American: ~22

## Scalp Biopsy

Terminal/vellus ratio

- Normal child:
  - Vellus>terminal initially with gradual transition to terminal>vellus at puberty.
  - Persistence ~6-21% vellus hairs late childhood
- Normal adult: 7:1
- Adult CTE: 9:1
- MPB (fully established): 2:1

## Scalp Biopsy

% Telogen

- Normal <10% (6.5%* normal adult) all areas of scalp
- Regional differences: frontal > occipital scalp regardless of age
- Relationship to:
  - Type of hair: Increase % telogen in thinner hairs
  - Age: Increase with aging in adults
  - CTE adults: 11%*
  - PHL adults: 16.8%*

* Whiting D. Derm Clinics 1996

Mean Inflammation and Fibrosis in Horizontal Sections of 4 mm Scalp Biopsy Specimens

| | Controls | Chronic Telogen Effluvium | Pattern Hair Loss |
|---|---|---|---|
| Mild I/F | 32% (7) | 28% (99) | 35% (142) |
| Moderate I/F | 9% (2) | 12% (44) | 37% (151) |
| Total patients with I/F | 41% (9) | 40% (143) | 71% (293) |
| Mild/moderate I/F ratio | 3.5:1 | 2.3:1 | 0.94:1 |
| Upper/lower follicular I/F ratio | 1.76:1 | 2.3:1 | 3.3:1 |

Whiting. J Am Acad Dermatol 1996; 35: 899-906.

## Treatment of Diffuse Hair Loss

- Identify cause and eliminate—time for regrowth is 6-12 months after resolution of problem, not from time of initiation of treatment
- Topical minoxidil: anagen promoter, off-label use, use until regrowth complete, use smaller amount and concentration for child to prevent systemic side effects
- Low level laser: low level irritation stimulates hair growth —no studies specifically in telogen effluvium, only AGA. Bought by patient online
- Medicated shampoos, topical ketaconazole

## Conclusions

- Diffuse hair loss in children has more confounding factors than that of adults
- Dietary and medication history is key
- Hair pull can help distinguish between TE, AGA, AA, LAS and SAS
- Biopsy can be helpful but not in itself usually diagnostic
- Replacement of deficient vitamins requires knowledge of interrelationship and potential effects on absorption