Guidelines for Diagnostic Evaluation in Cicatricial Alopecia

Ralph M. Trüeb, M.D.
Center for Dermatology and Hair Diseases
Bahnhofplatz 1A
8304 Wallisellen (Zurich)
Switzerland

www.derma-haarcenter.ch
"If a man's hair has fallen from his head, he is bald but he is clean.

And if a man's hair has fallen from his forehead and temples, he has baldness of the forehead but he is clean.

But if there is on the bald head or the bald forehead a reddish-white diseased spot, it is leprosy (tzaraath, צורע) breaking out on his bald head or his bald forehead.

In that case the priest shall examine him, ..."
Androgenetic Alopecia

Genetically determined, androgen induced, age-dependent progressive hair loss with sex-dependent differences in incidence, pattern and severity, characterized by

- typical bitemporal recession of hair and balding vertex in men and diffuse thinning of the crown with an intact frontal hairline in women
- diversity of hair shaft diameter (anisotrichosis) on dermoscopic examination
- hair follicle miniaturization on histopathologic examination

Accounts for > 80% of dermatologic consultations for hair loss
Cicatricial Alopecia

Diverse group of disorders that cause permanent destruction of the pilosebaceous unit and irreversible hair loss, characterized by

• visible loss of follicular ostia
• destruction of the hair follicle on histopathologic examination
• irreversibility of a potential disturbing cosmetic defect

Accounts for < 5% of dermatologic consultations for hair loss
Step 1. Regognizing Cicatricial Alopecia

Relatively rare: Account for 3-7 % of dermatologic consultations for hair loss

Irreversibility

Disturbing cosmetic defect

May be due to a serious underlying disease, e.g. autoimmune, deep infectious, metastatic or primary neoplastic disease

Diagnostic and therapeutic problems

Cicatricial Alopecia

Diagnostic Problems:

- Many have neither known cause nor consistent clinicopathologic findings
- Clinical inspection often of limited usefulness for diagnosis
- Inconsistent use of terminology with an apparent maze of different entities:
  - number of different terms to denote same entity
  - single term to denote different entities

Therapeutic Problems:

- Patients‘ delay, when irreversible scarring has occurred
- The goal of therapy is mostly to halt further progression
- Since the causes are mostly unknown, therapy has remained empiric and nonspecific
- Published data on therapies have low levels of evidence

Diagnostic Problems: Scalp Biopsy

Frequent problems related to the scalp biopsy are the reluctance of many dermatologists to perform a scalp biopsy and therefore lack of experience with the proper procedure.

Inadequate biopsies:

- superficial (without subcutaneous tissue)
- small
- tangential to hair follicles
- with crush artefacts
- at inappropriate site

The hair follicle and its derangements are complex and dynamic, while a biopsy only gives a momentary snap-shot of the pathology.

Eventually, the underlying process ends in a common final pathway of replacement of follicle by fibrous tissue.

Finally, many pathologists lack familiarity with scalp histopathology.
Step 2. Performing an Appropriate Scalp Biopsy

For a biopsy an area of the scalp is chosen where the disease is active, while areas should be avoided where no hair follicles are present.

The scalp specimen obtained for histopathologic study should be large enough to include multiple hairs, deep enough to contain the hair bulb, and properly angled so that microscopic sectioning shows the entire follicular structure.

• Two 4- to 6-mm-Punch biopsies
  • from the margin of the involved area
  • placed parallel to the emerging angle of the hair stubbles
  • turned through the dermis and subcutaneous fat to a level including the hair bulbs

• One half of the specimen is submitted for the routine hematoxylin and eosin examination
• The other half for immunofluorescence studies as indicated
• Transverse sectioning of a second, entire punch may be done for quantitative morphometric analyses of the follicles and hair.

Step 3. Understanding the Pathobiology of Cicatricial Alopecia

Genetic derangement of hair follicle development:

- Defective gene important to cycle control or lineage differentiation

or

Acquired, irreparable destruction of critical hair follicle structures (follicular sheath, follicular papilla), or of the whole hair follicle:

- stem cell depletion
- aberrant fibrous reaction
- loss of proper hair follicle architecture preventing interaction of follicular papilla and stem cells
- primary vs. secondary cicatricial alopecia

Genetic/Developmental Defects (Rare)

Aplasia cutis congenita
Epidermal nevus
Incontinentia pigmenti Bloch-Sulzberger
Alopecia in patient with GABEB
Alopecia ichthyotica (in lamellar ichthyosis)
Step 4. Making a Distinction between Primary and Secondary Cicatrical Alopecia

**Secondary cicatrical alopecia:**

Results from destructive cutaneous disease in which the follicle is destroyed in a non-specific manner:

- **trauma** (chemical, physical)
- **infection** (fungal, bacterial, viral)
- **infiltration** (granulomatous, neoplastic)
- **autoimmune** (circumscribed scleroderma, cicatricial pemphigoid, temporal arteritis)

**Primary cicatrical alopecia:**

Target of inflammation and destruction is the follicle

Cause mostly unknown, **classification on the basis of inflammatory infiltrate**:

- lymphocytic
- neutrophilic
- mixed

Diagnostic Flow Chart for Cicatrical Alopecia

Late-stage Disease (Pseudopelagic State)

Secondary Cicatricial Alopecias

Primary Cicatricial Alopecias

Start

Follicular orifices?

LOST

BIOPSY

Secondary cause?

NO

Inflammation?

YES

Elastin stain

LOSS/ABNORMAL FIBRES

NORMAL FIBRES

Superficial wedge-shaped scar

Inter-follicular elastin normal

Elastic fibres absent from fibrous tracts and inter-follicular dermis

Thickened elastin fibres

Broad fibrous tracts/intact elastic sheath

Not PCA

LPP

CCLE FD DCS AKN ANV EPD

CCCA PB

Predominant cell type?

Lymphocytes

Neutrophils/Mixed

Sarcoidosis

Scalp Metastasis

Pemphigoid

Angiosarcoma

Temporal Arteritis

Primary B-Cell Lymphoma
Step 5: Working Classification for Primary Cicatricial Alopecia

**Lymphocytic:**
- Chronic cutaneous lupus erythematosus
- (Classic) Lichen planopilaris and variants:
  - Disseminated (Lassueur-Graham-Little)
  - Patterned (FFA, FAPD)
- (Classic) Pseudopelade of Brocq
- Alopecia mucinosa
- Central centrifugal cicatricial alopecia?

**Neutrophilic:**
- Folliculitis decalvans (Quinquaud) and variants:
  - Tufted hair folliculitis (Sanderson and Smith)
- Dissecting cellulitis (Hoffmann)

**Mixed:**
- (KFSD/Folliculitis spinulosa decalvans)
- Folliculitis (acne) keloidalis (nuchae)
- Folliculitis (acne) necrotica (varioliformis/miliaris)
- Erosive pustular dermatosis (of the scalp)

**Non-specific cicatricial alopecia**

---

Olsen et al. Summary of NAHRS-sponsored workshop on cicatricial alopecia. JAAD 2003;48:103-10
Primary Cicatricial Alopecias

University Hospital of Zurich Department of Dermatology:
136 scalp biopsies for histology and DIF. Definitive diagnosis in 126/136:

- 28 % (35/126) *lichen planopilaris* (LPP)
- 23 % (29/126) *chronic cutaneous lupus erythematosus* (CCLE)
- 21 % (27/126) *folliculitis decalvans* (FD)
- 10 % (13/126) *pseudopelade of Brocq* (PB, criteria of Braun-Falco)

In 97 % (122/126) definitive diagnosis on the basis of histology alone:

- in 94 % (33/35) of LPP
  - DIF: sensitivity 34 %, specificity 98 %
- in 93 % (27/29) of CCLE
  - DIF: sensitivity 76 %, specificity 96 %

Cytoid bodies in groups > 5

Lupus band test

Primary Cicatricial Alopecias: Overview

Lymphocytes

Interface changes?

YES

NO

Lichenoid or vacuolar?

VACUOLAR

LYMPHOCYTES

Mucin stain

NEGATIVE

POSITIVE

Mucin in ORS and Sebaceous glands

See Table 3

Sinus tracts?

PRESENT

NEGATIVE

PAS stain

SPORES/HYPHAE

Tinea capitis

Neutrophils/Mixed

Sinus tracts?

ABS

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?

PRESENT

Sinus tracts?

NEGATIVE

Sinus tracts?
Step 6. Excluding an Infectious Pathogen: Tinea capitis

Infectious disease of scalp due to dermatophytes of *Microsporum* or *Trichophyton* genus

Clinical presentations (highly variable!):
- superficial-aphlegmatic
- superficial-inflammatory
- deep-inflammatory

Investigations (be suspicious!):
- clinical suspicion
- Wood lamp examination
- microscopic examination of KOH preparation
- cultural identification

Treatment (always systemic!):
- itraconazole 5mg/kg or fluconazole 6 mg/kg for 6 weeks
- + topical antimycotic/sporocidal shampoo
- + prednisone 1 mg/kg 1-2 week in case of deep inflammation (Kerion)
- + hygienic measures (according to identified fungus)
Excluding an Infectious Pathogen: Folliculitis Decalvans

Adults

Central scalp > grouped follicular pustules, miliary abscesses at hair-bearing margin

*Staph. aureus* are pathogenic

Association with seborrhoic dermatitis:  
*Cicatrizizing seborrhoic eczema (Laymon, 1947)*

Hair tufting may be pronounced:  
*Tufted hair folliculitis*

Very rare association with immune deficiency

**Treatment:**

- rifampicin 2 x 300 mg  
  + clindamycine 2 x 300 mg 10 weeks
- other antibiotic protocols

Differential Diagnosis: Dissecting Cellulitis of the Scalp

Black males >

painful, boggy, contiguous dermal alopecia nodules that can spontaneously suppurate, sinus tracts

Non-scalp involvement: follicular occlusion triad:
• acne conglobata
• pilonidal sinus

Treatment:
• isotretinoin 1mg/kg 6 months + erythromycine 4 x 500 mg 4 weeks + intralesional corticosteroids, or
• dapsone 100-200 mg/day + zink sulfate 2 x 200 mg/day
• drainage of abscesses
• radical surgical resection
• laser-assisted epilation

Folliculitis Keloidalis

Black males >

Occipital scalp, firm red-brown papules, papulopustules, nodules and keloidal plaques

Non-scalp involvement absent

**Treatment:**
- minocycline 100 mg/day
- intralesional corticosteroids
- antiseptic shampoo
- omit shaving neck
- laser vaporisation

Step 7. Excluding Systemic Disease: Chronic Cutaneous (Discoid) Lupus Erythematosus

Females >

Symptomatic, erythematous scaly plaques with follicular plugs, telangiectases, atrophy and depigmentation with time, activity in center of alopecic patch

Non scalp disease may be present:
• acute cutaneous LE
• subacute cutaneous LE
• chronic cutaneous LE
• rule out systemic disease (ACR criteria)!

Treatment:
• antimalarials
• topical corticosteroids
• azathioprine or mycophenolate mofetil
Lupus Erythematosus: Non Scalp Disease

- **Acute cutaneous LE**: ACR criteria fulfilled in 100%
- **Subacute cutaneous LE**: ACR criteria fulfilled in ca. 50%
- **Chronic cutaneous LE**: ACR criteria fulfilled in <10%
Differential Diagnosis: (Classic) Lichen planopilaris

Females >

Pruritic central or multifocal alopecic patches with follicular hyperkeratosis and erythema at hair-bearing margin

**Non scalp involvement** may be present:
- mucosal membranes
- glabrous skin
- nails

**Treatment:**
- topical corticosteroids
- systemic corticosteroids
- oral doxycycline or hydroxychloroquine
- azathioprine, mycofenolat mofetil, or cyclosporine A
- pioglitazone
(Classic) Lichen planopilaris: Non Scalp Involvement

- Reticular LP (Wickham’s striae)
- Atrophic LP (desquamative gingivitis)
- Leukoplakic LP
- Erosive-ulcerative LP
(Classic) Lichen planopilaris: Non Scalp Involvement

- **Lichen planus**
- Köbner's
- Genital (annular)
- Nail (pterygium)
- Ulcerative palmoplantar
Lichen planopilaris: Variants

**Disseminated:**

**Lassueur-Graham Little syndrome (1930)**
Patches with follicular keratosis
Associated nonscarring alopecia in axillae, pubic area

**Patterned:**

**Frontal fibrosing alopecia (Kossard, 1994)**
Postmenopausal >
Frontotemporal recession often with classic LPP a hair-bearing margin
Involvement of eyebrows in ca. 50%
Involvement of body hairs often unnoticed

**Fibrosing alopecia in a pattern distribution**
(Zinkernagel and Trüeb, 2000)
Primary Cicatricial Alopecias

- Lympho-cytic
  - LPP
  - LPP variants
  - DLE
  - A. mucinosa

- Neutrophilic
  - FD
  - FD variants
  - DC

- Mixed
  - KFSD/FSD
  - FK
  - FN
  - EPD

Secondary Cicatricial Alopecias

- Trauma (chemical, physical)
- Infection (fungal, bacterial, viral)
- Granulomatous infiltration
- Neoplastic infiltration
- Autoimmune (circumscribed scleroderma, cicatricial pemphigoid, arteritis temporalis)

Pseudopeladiac State of Degos

- Pseudopelade Brocq
- ?
- Central Centrifugal Scarring Alopecia: Hot Comb Alopecia/FDS
- DC

Alopecia parvimalculata Dreuw (children)
(Classic) Pseudopelade Brocq

Adults

Asymptomatic, noninflammed, ivory-white or flesh colored small oval-round, reticulate, or large, irregular patches ± atrophy

Non-scalp involvement absent

Histopathology: Selective loss of hair follicles (indistinguishable from end-stage lichen planopilaris)

Some experts suggest LPP and PPB are not distinct diseases, but rather different clinical presentations in a spectrum derived from the same underlying pathogenic mechanism.

Thank you for your attention!