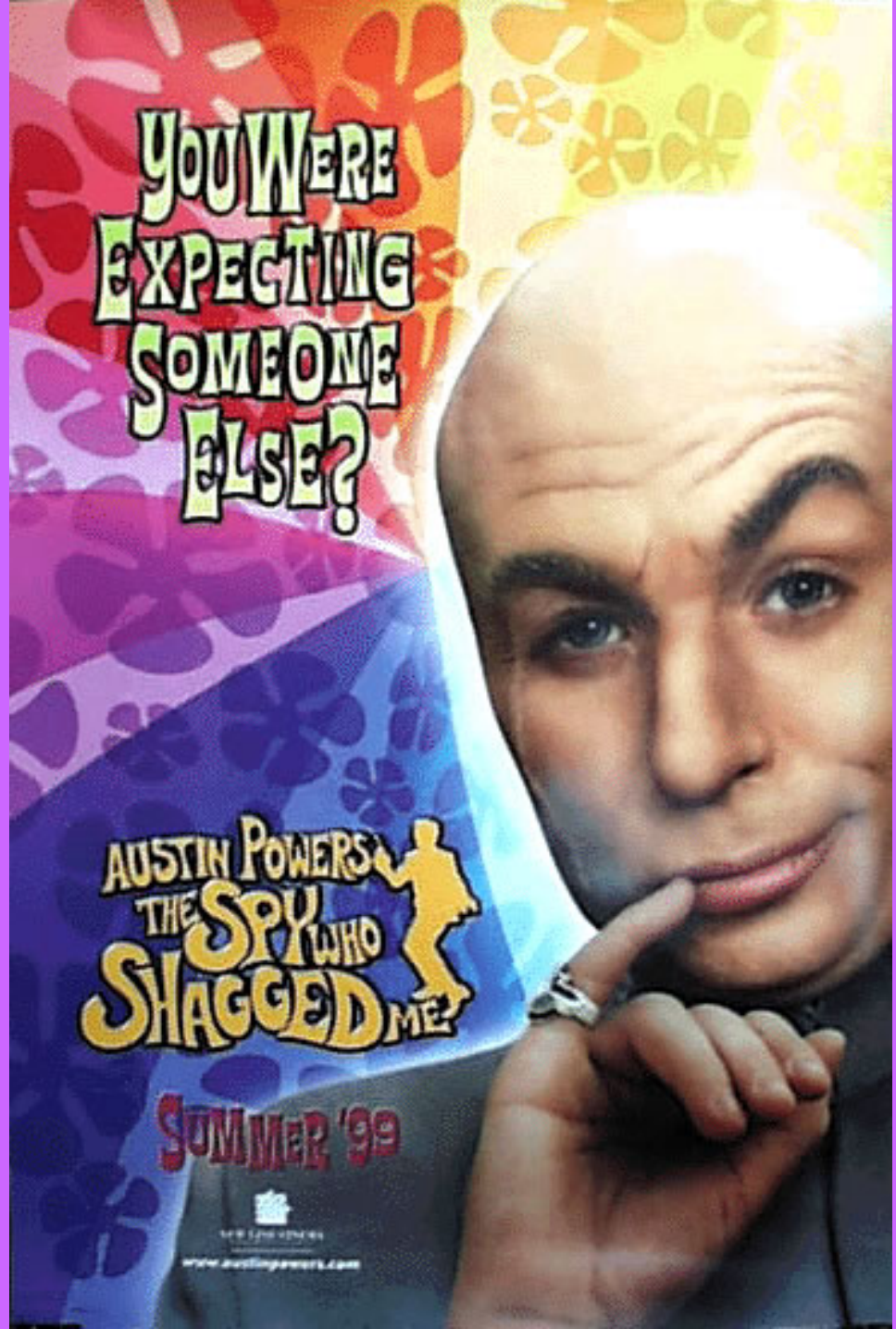
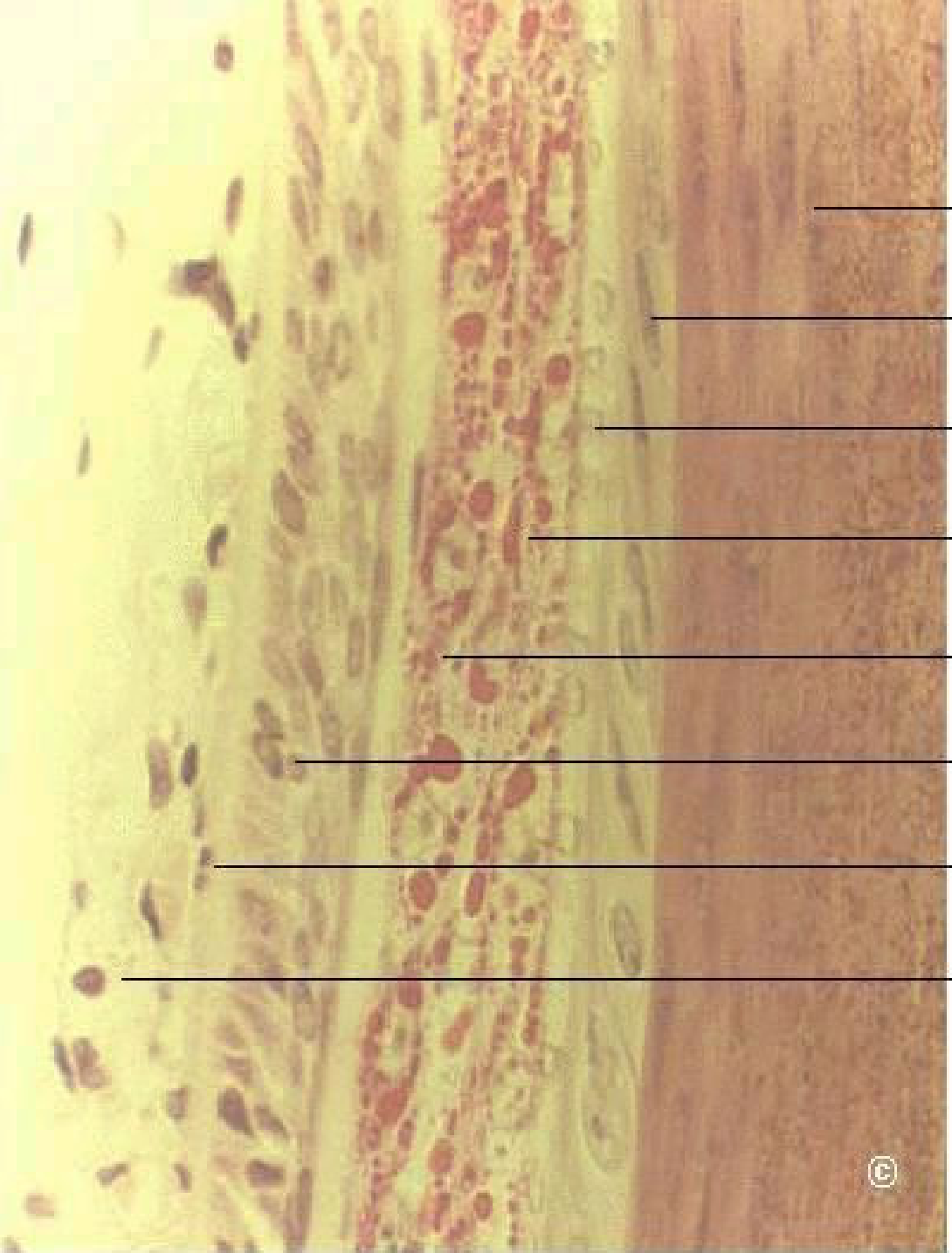
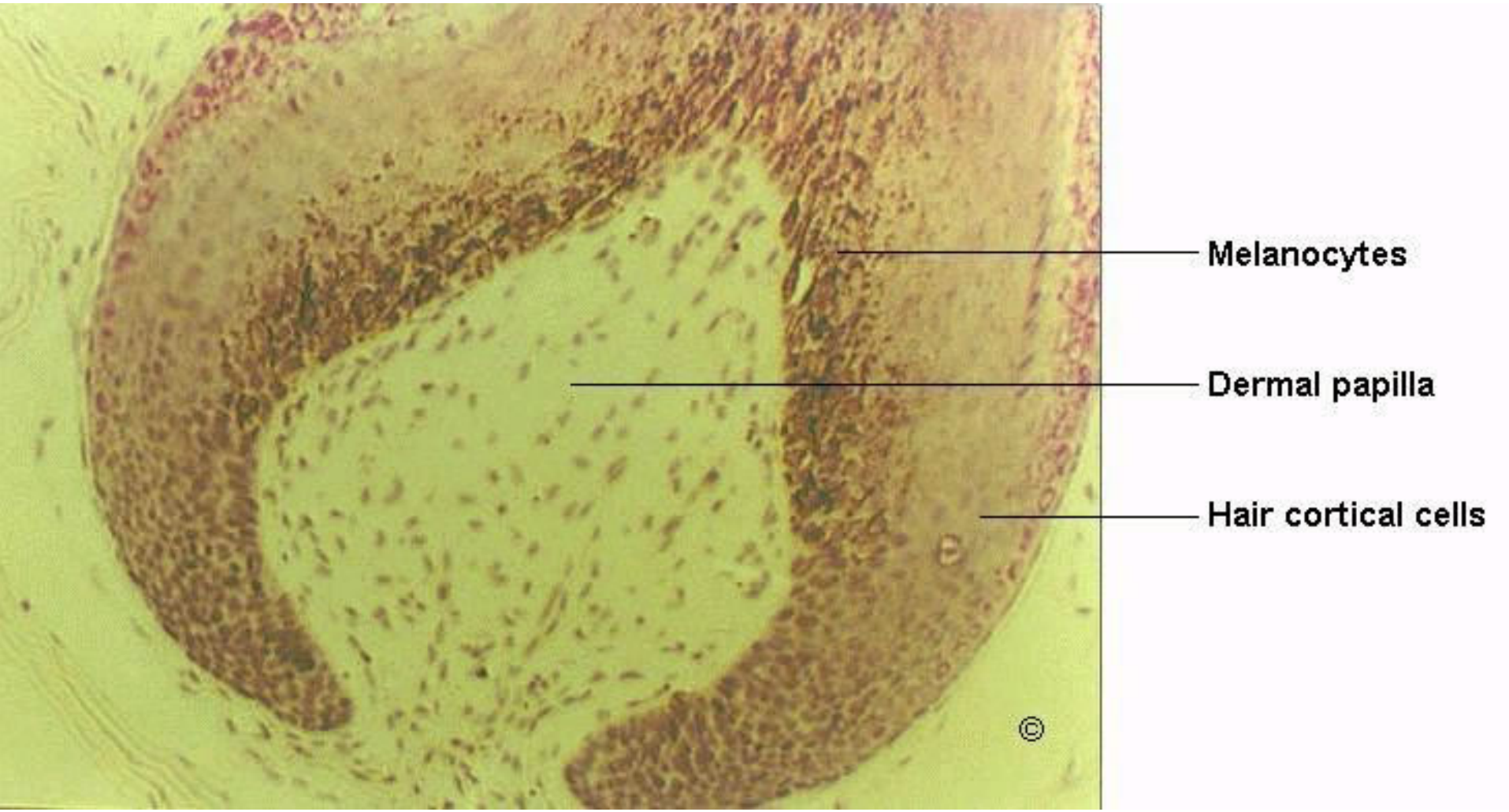
Alopecia-Don't Be in a Hairy To Make the Diagnosis!

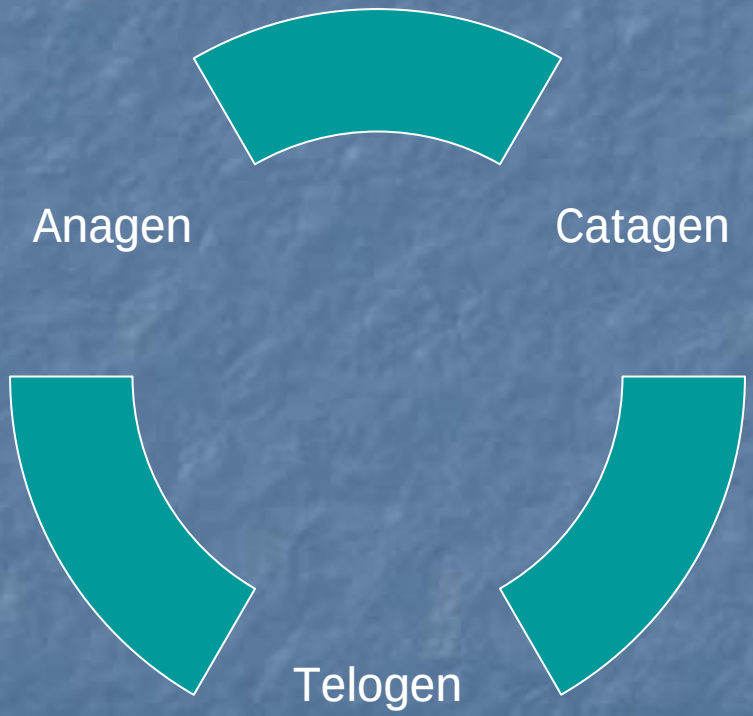
Paul K. Shitabata, M.D.
Dermatopathologist
APMG


YOU WERE EXPECTING SOMEONE ELSE?
AUSTIN POWERS
THE SPY WHO SHAGGED ME
SUMMER '99

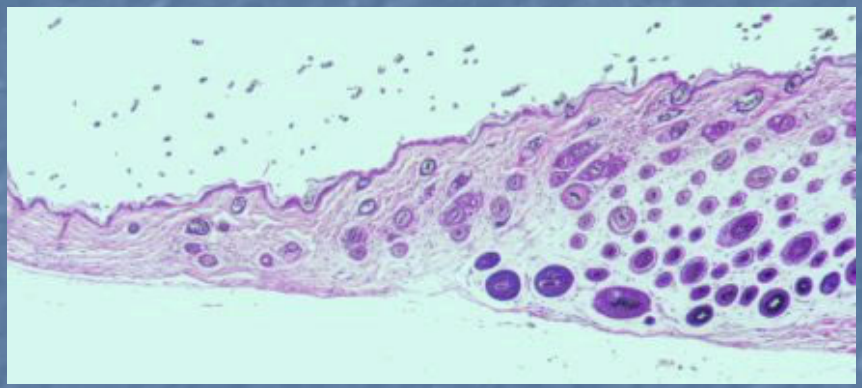

Hair cortex
Hair cuticle
Inner root sheath cuticle
Inner root sheath Huxley layer
Inner root sheah Henle layer
Outer root sheath
Basment membrane
Dermal sheath
©

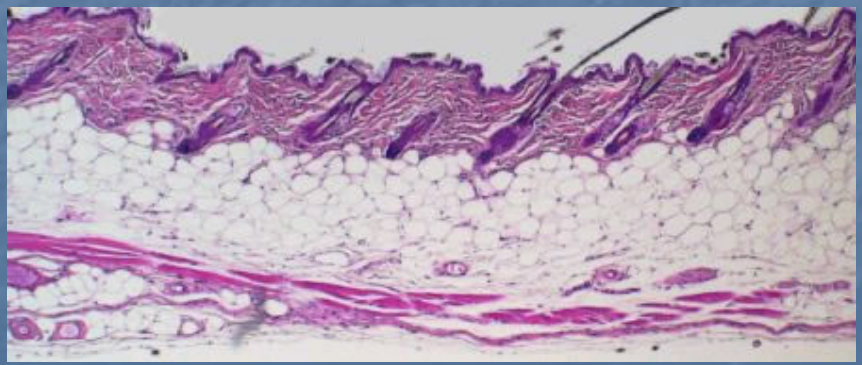

Melanocytes
Dermal papilla
Hair cortical cells

Hair Cycle



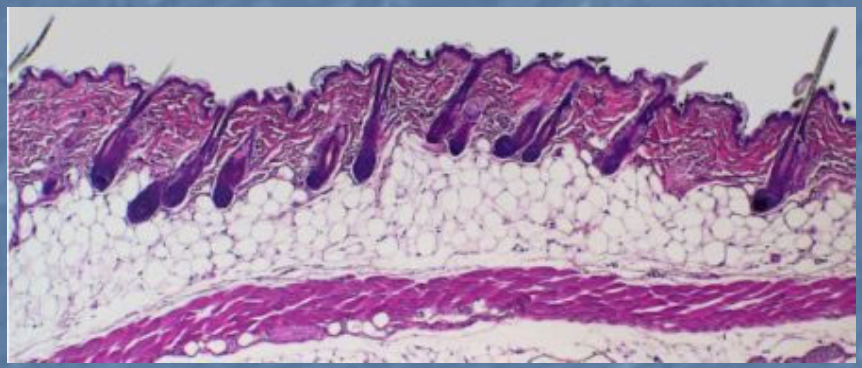
Hair Cycle





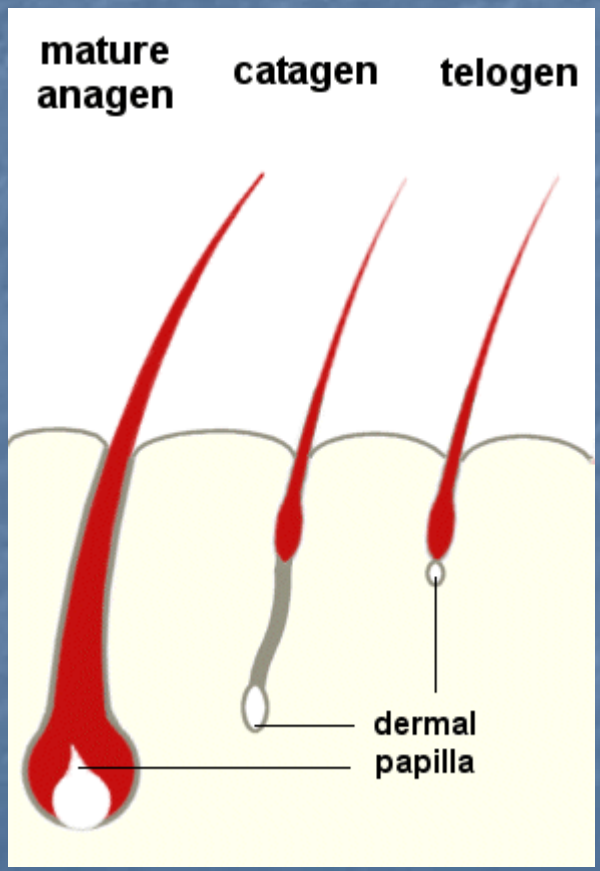
- Complete cycle
  - Anagen-catagen-telogen
- Telogen
  - Several factors can influence and inhibit hair production and in some cases lead to physical destruction of the hair follicle
  - Adverse reactions to drugs and cosmetics, scarring, tumors, radiation, the genetics of the individual, hormones and/or their immune system

Hair Cycle



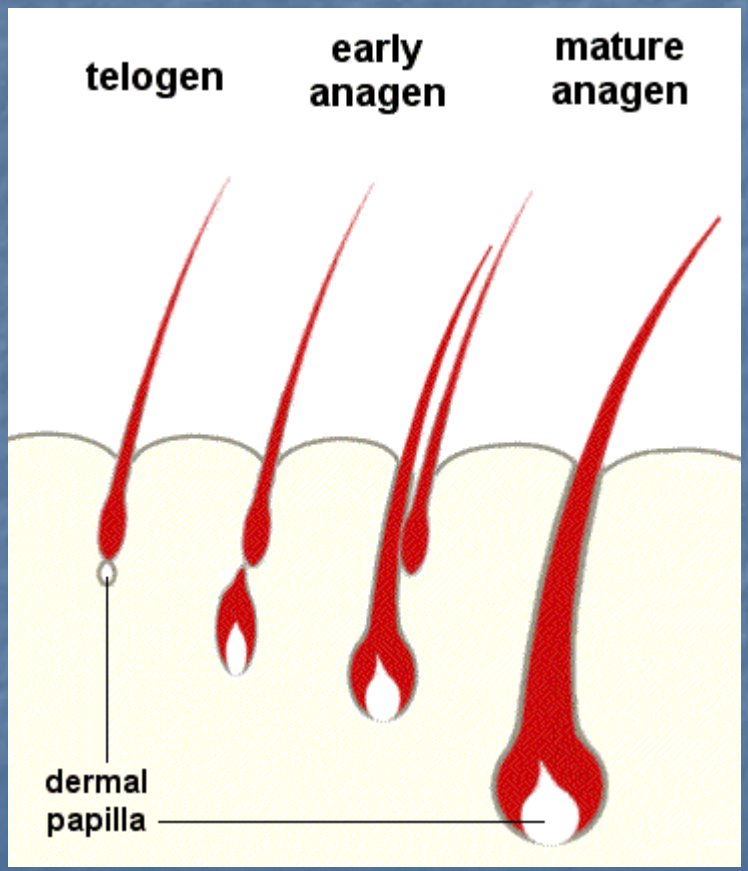
- Anagen is the longest phase
  - Up to 90% of follicles on a normal human scalp in this active hair growth state at any given time
  - Length of the anagen growth phase for scalp hair is usually 6-10 years
- Telogen hair follicles 10%
  - Lasts just 30-90 days
- Catagen estimated at 14-21 days
- Average rate of hair fiber growth is around 0.35mm a day
  - Varies depending on the site of the hair follicle, age and sex

Hair Cycle



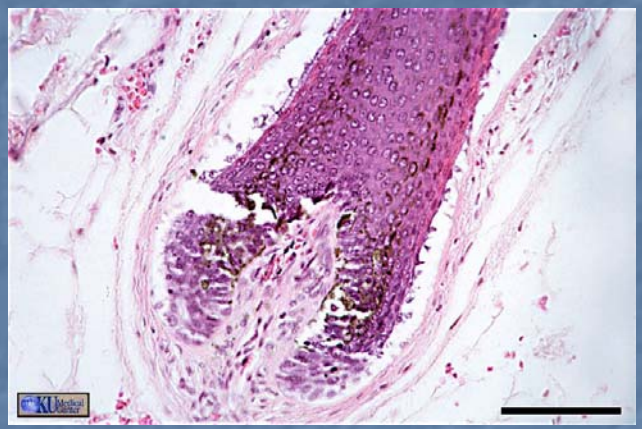
- Regression of a mature anagen hair follicle
- Entering catagen the dermal papilla condenses as the cells become inactive
- With a lack of dermal papilla cell stimulation, the hair fiber and root sheaths stop growing
- In telogen the dermal papilla can become isolated in the dermis and the hair fiber can easily be pulled out (by combing, shampooing, or brushing)

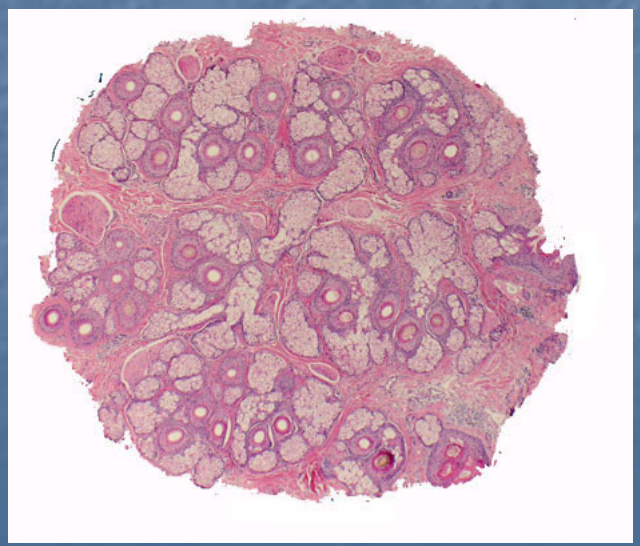
Hair Cycle



- Diagram showing a resting hair follicle returning from resting telogen to growing anagen
- If the old fiber has not already fallen out it is pushed out by the new hair fiber growing underneath

Biopsy

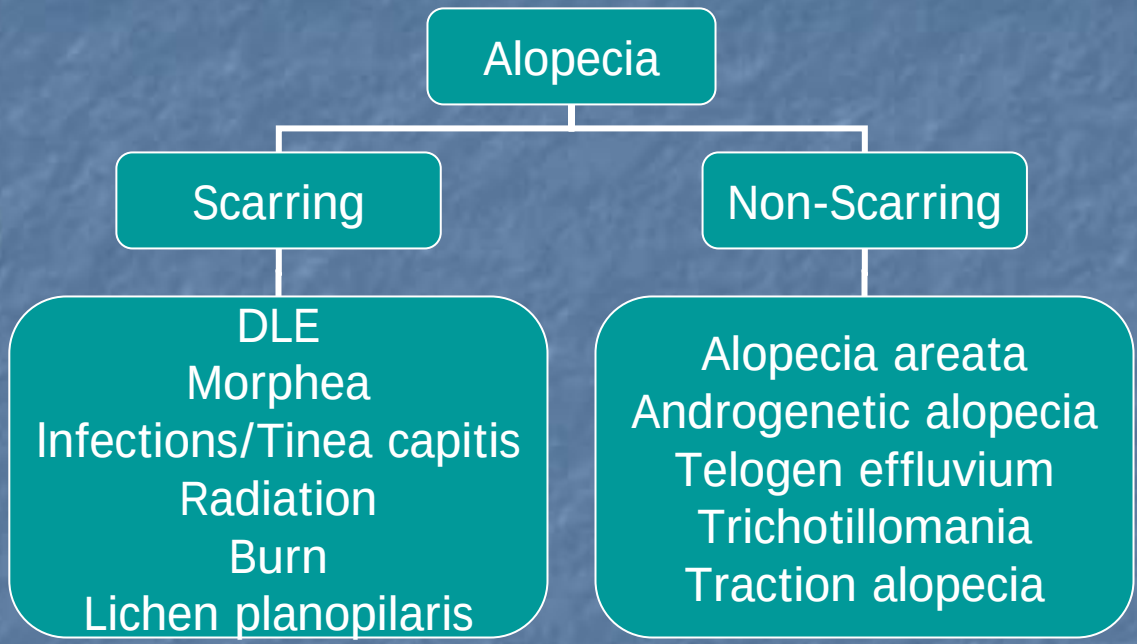


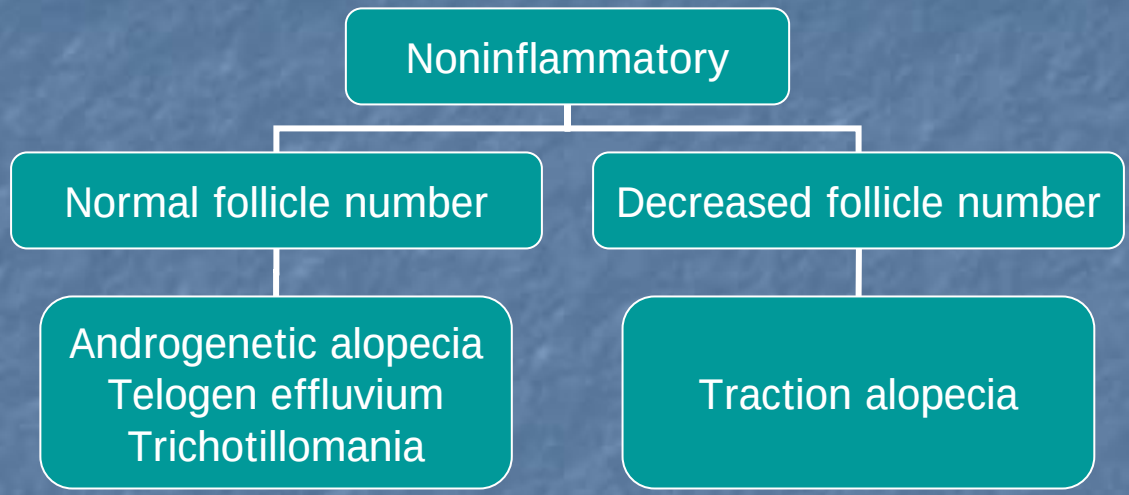


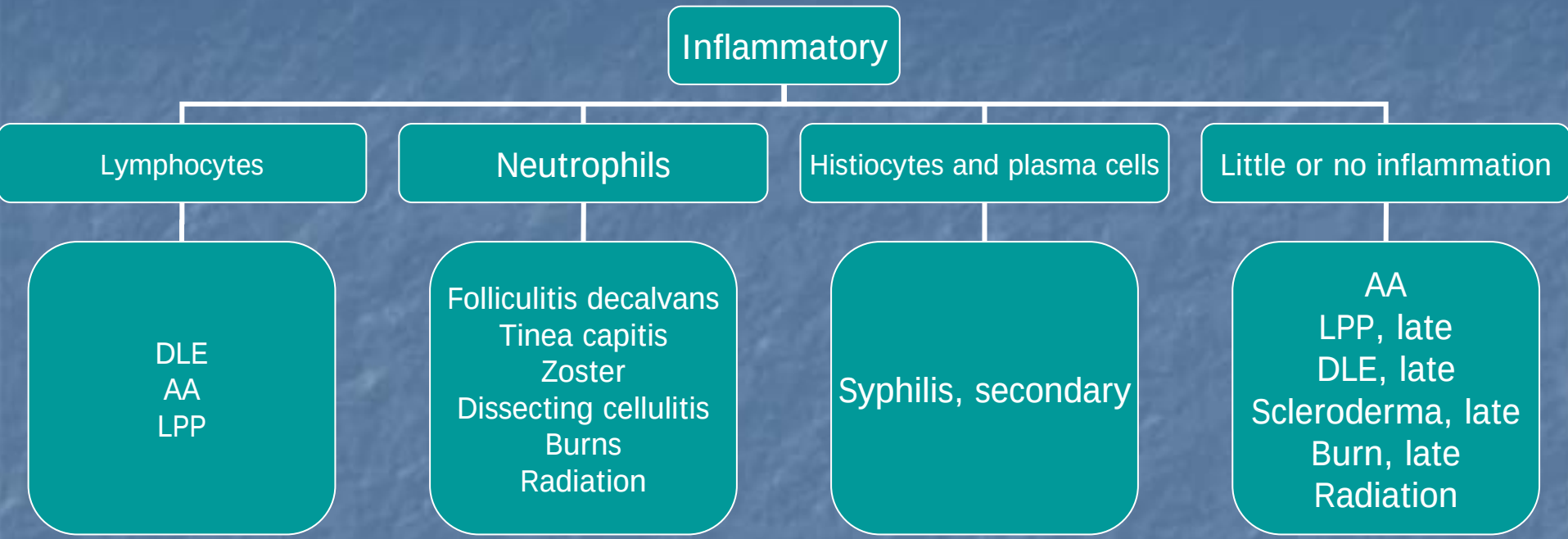
- Vertical
- Horizontal

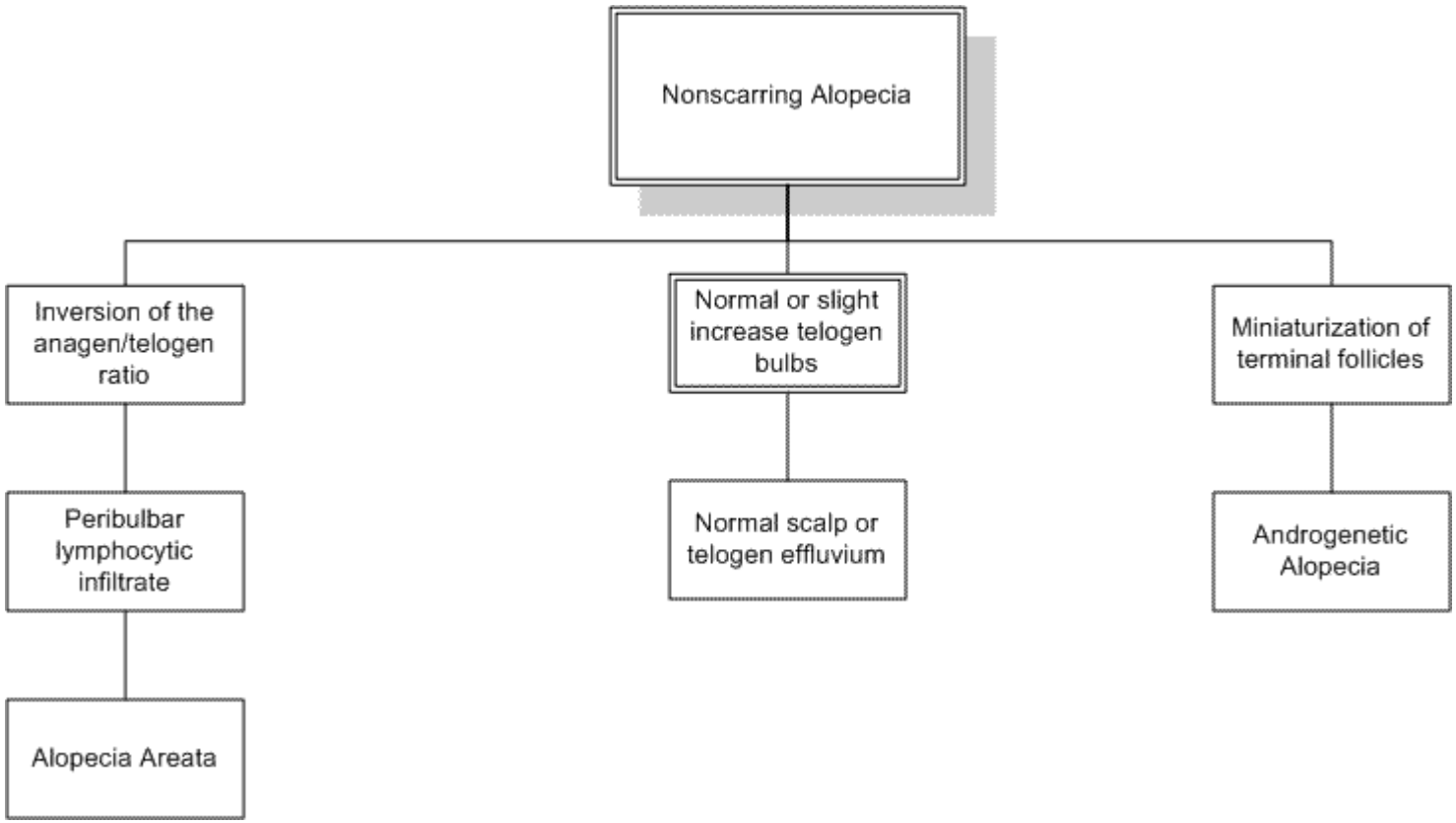
Adjuvant Studies

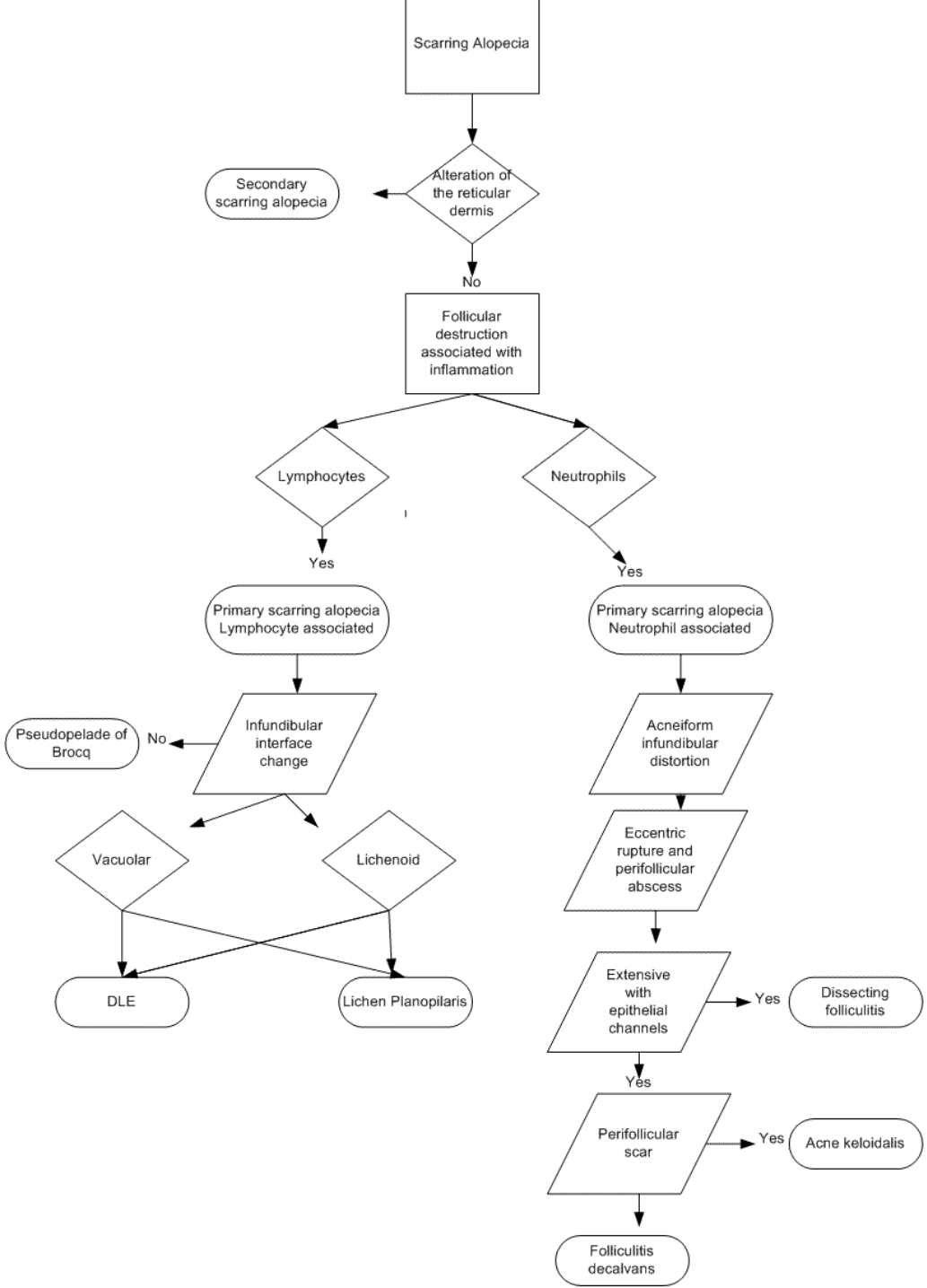
- Elastic stain
- Trichrome stain
- PAS

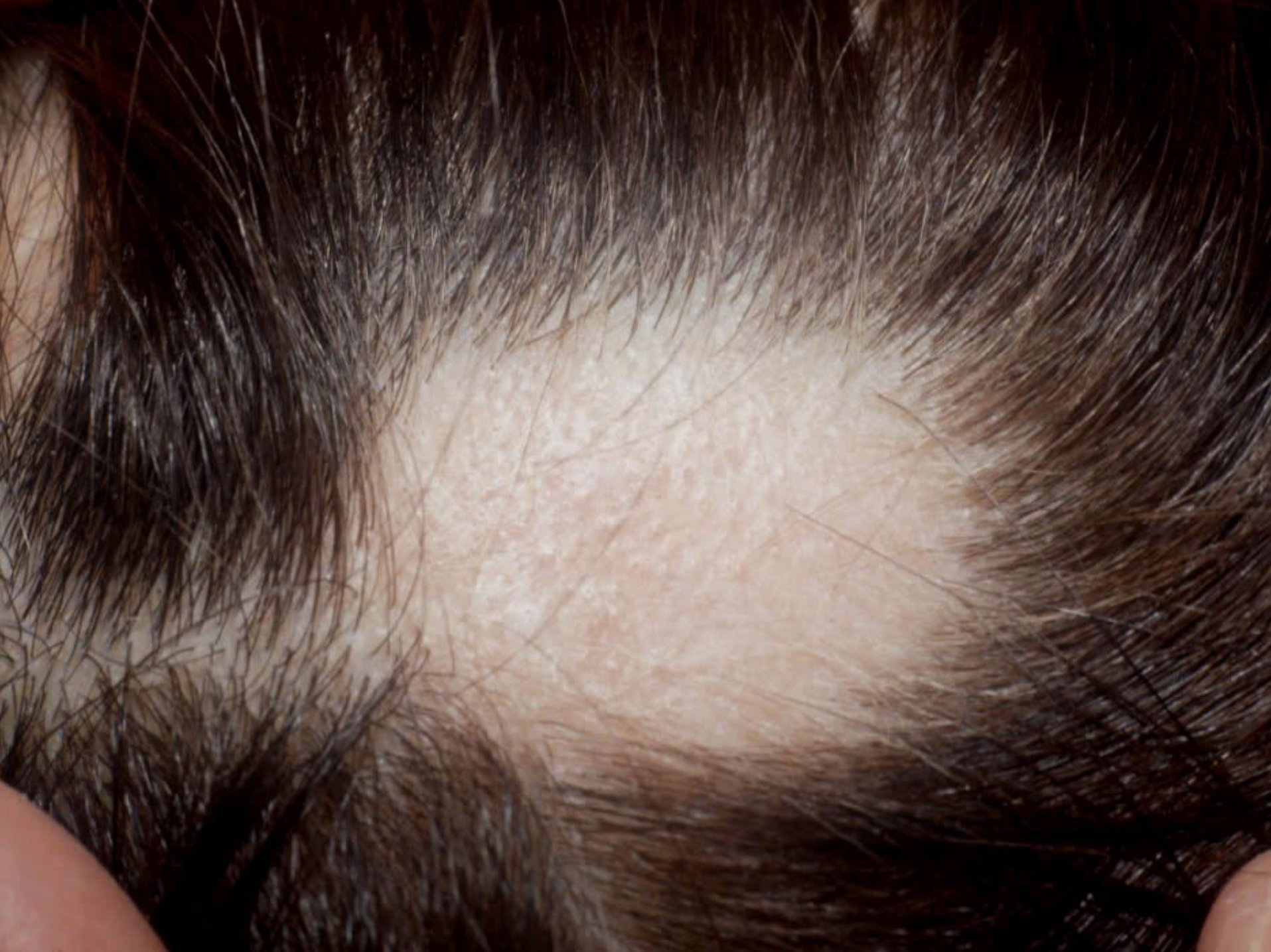

Alopecia
Scarring
Non-Scarring
DLE
Morphea
Infections/Tinea capitis
Radiation
Burn
Lichen planopilaris
Alopecia areata
Androgenetic alopecia
Telogen effluvium
Trichotillomania
Traction alopecia

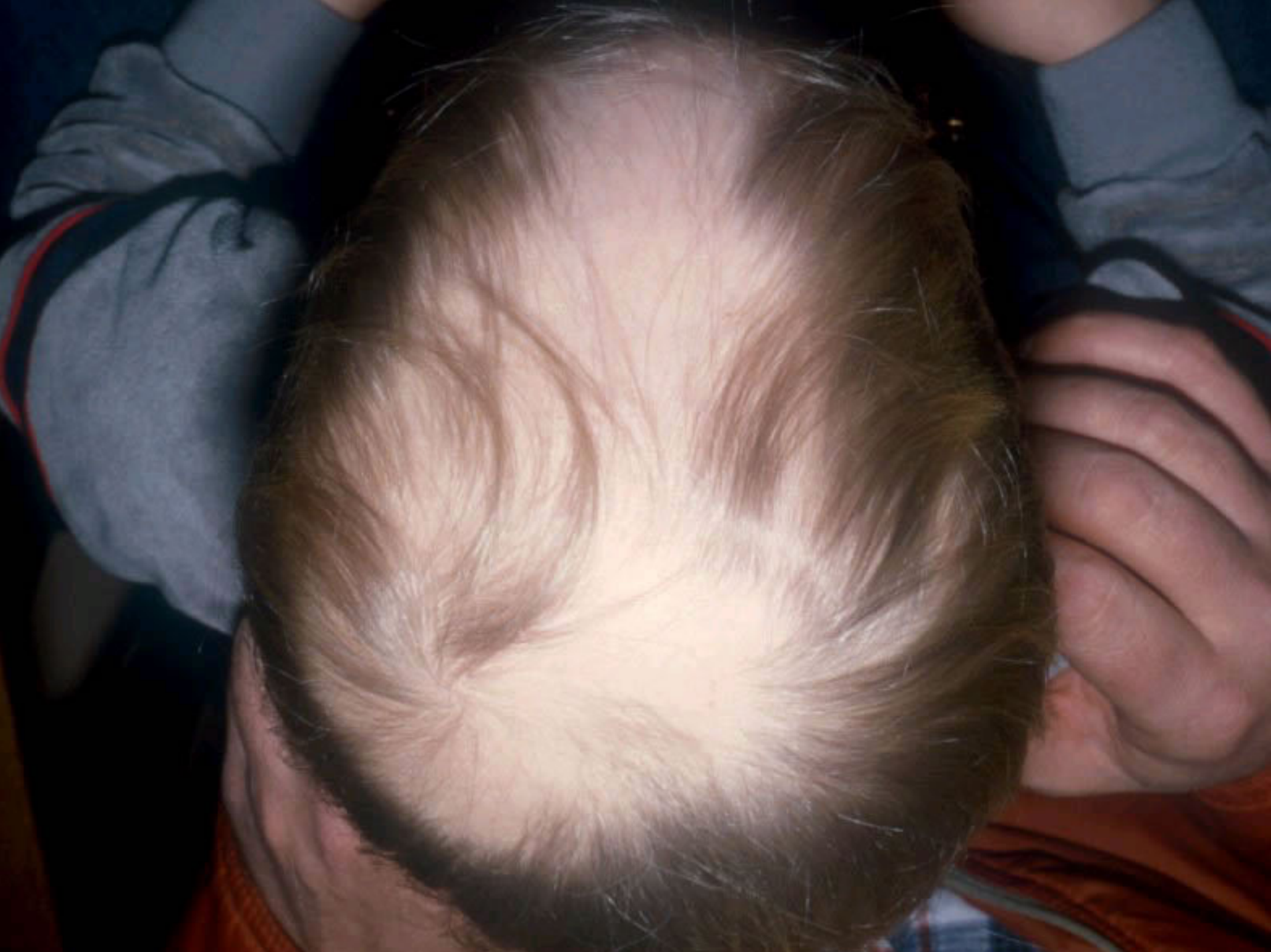

Noninflammatory
Normal follicle number
Decreased follicle number
Androgenetic alopecia
Telogen effluvium
Trichotillomania
Traction alopecia

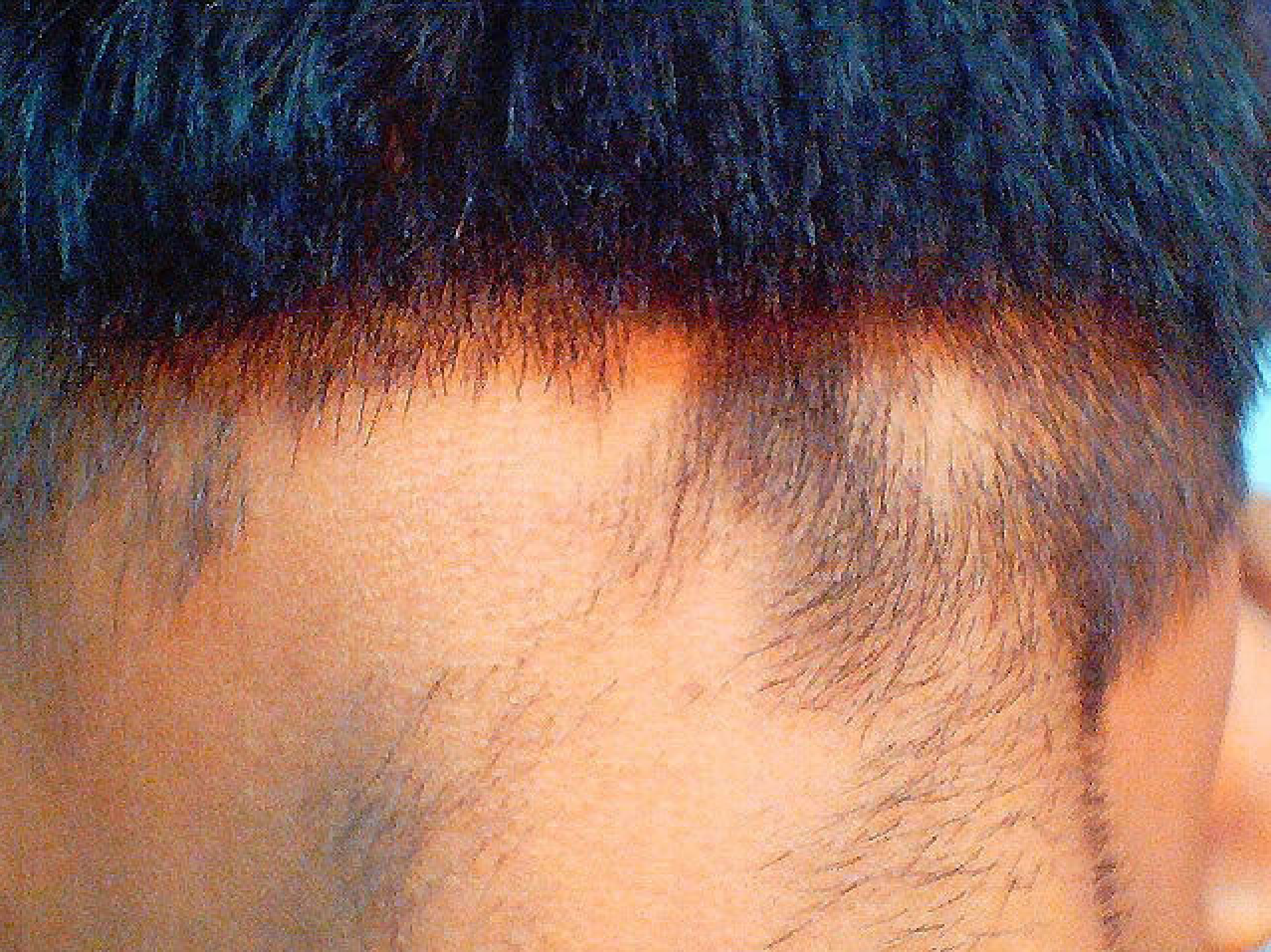

Inflammatory
Lymphocytes
Neutrophils
Histiocytes and plasma cells
Little or no inflammation
DLE
AA
LPP
Folliculitis decalvans
Tinea capitis
Zoster
Dissecting cellulitis
Burns
Radiation
Syphilis, secondary
AA
LPP, late
DLE, late
Scleroderma, late
Burn, late
Radiation

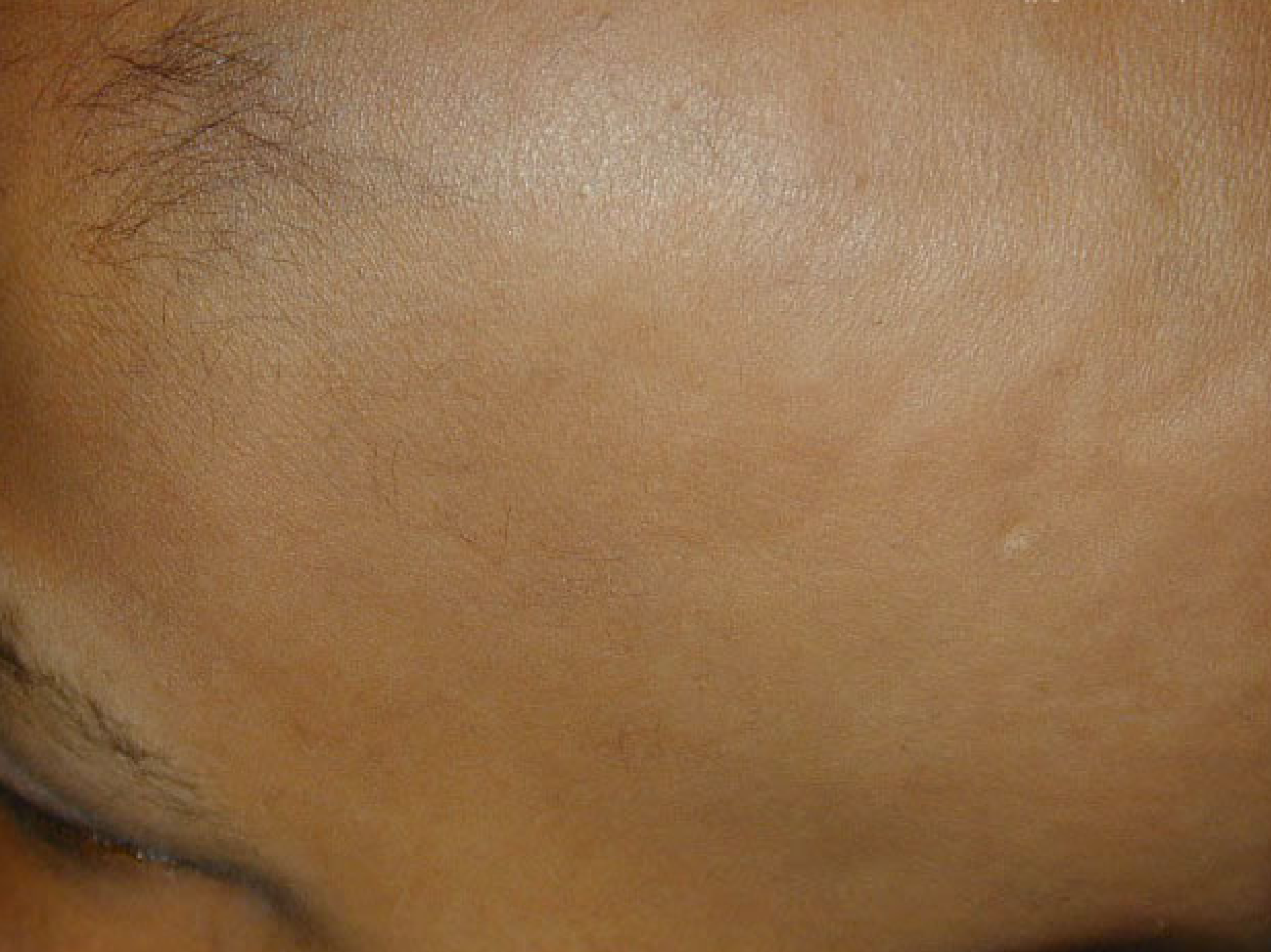

Nonscarring Alopecia
Inversion of the anagen/telogen ratio
Peribulbar lymphocytic infiltrate
Alopecia Areata
Normal or slight increase telogen bulbs
Normal scalp or telogen effluvium
Miniaturization of terminal follicles
Androgenetic Alopecia

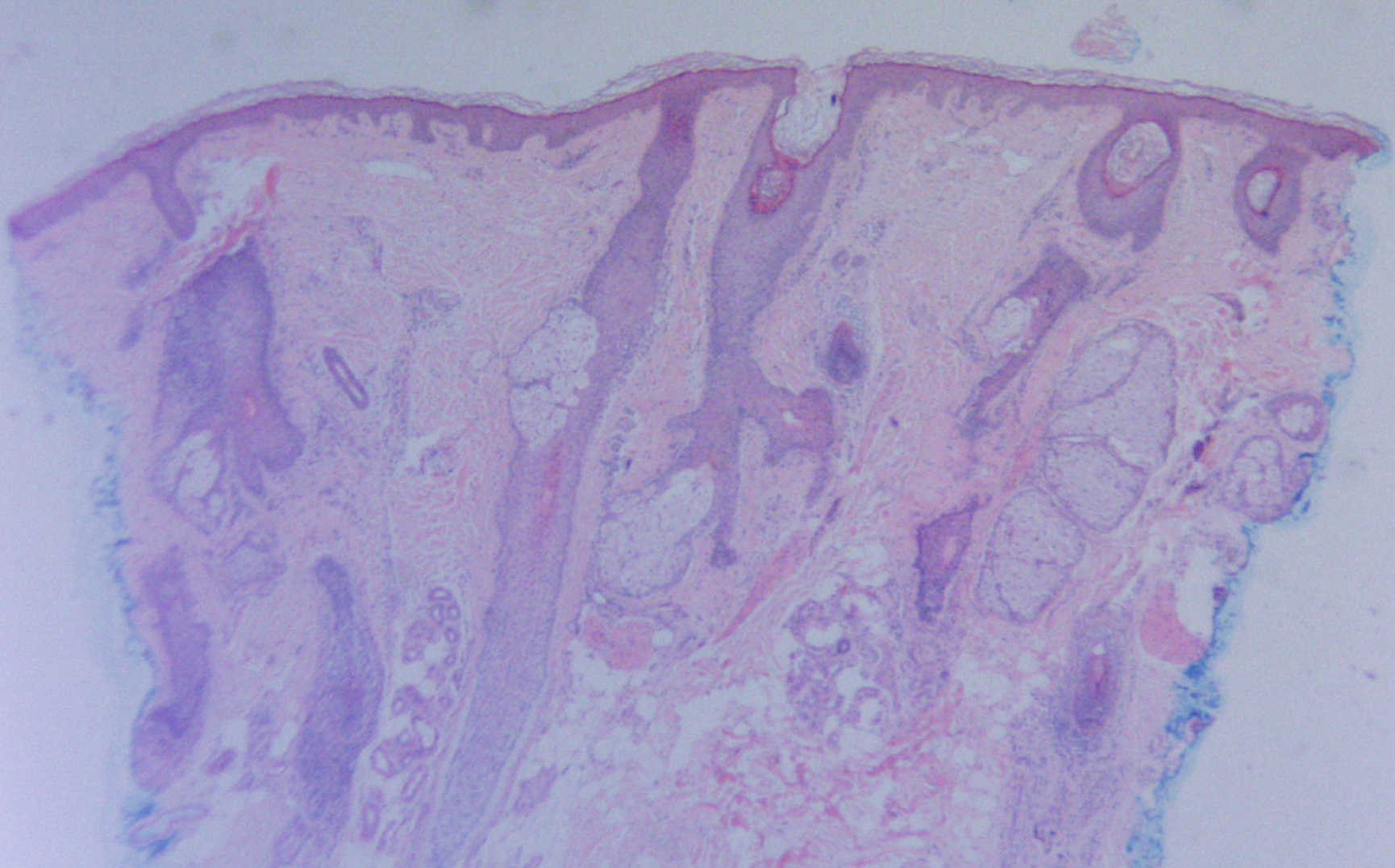

Scarring Alopecia
Alteration of the reticular dermis
Secondary scarring alopecia
No
Follicular destruction associated with inflammation
Lymphocytes
Neutrophils
Yes
Yes
Primary scarring alopecia Lymphocyte associated
Primary scarring alopecia Neutrophil associated
Infundibular interface change
No
Pseudopelade of Brocq
Vacuolar
Lichenoid
DLE
Lichen Planopilaris
Acneiform infundibular distortion
Eccentric rupture and perifollicular abscess
Extensive with epithelial channels
Yes
Dissecting folliculitis
Yes
Perifollicular scar
Yes
Acne keloidalis
Folliculitis decalvans

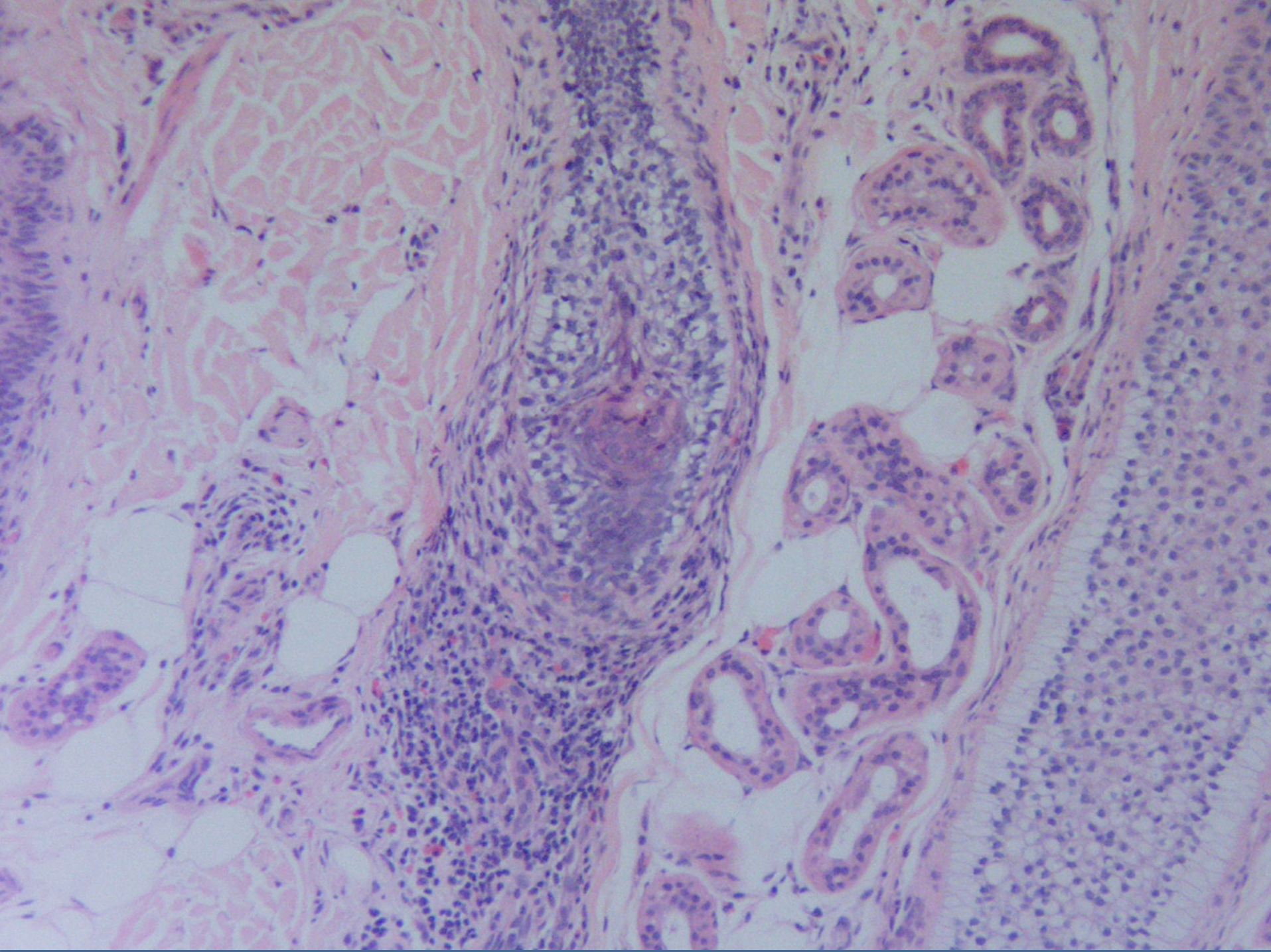


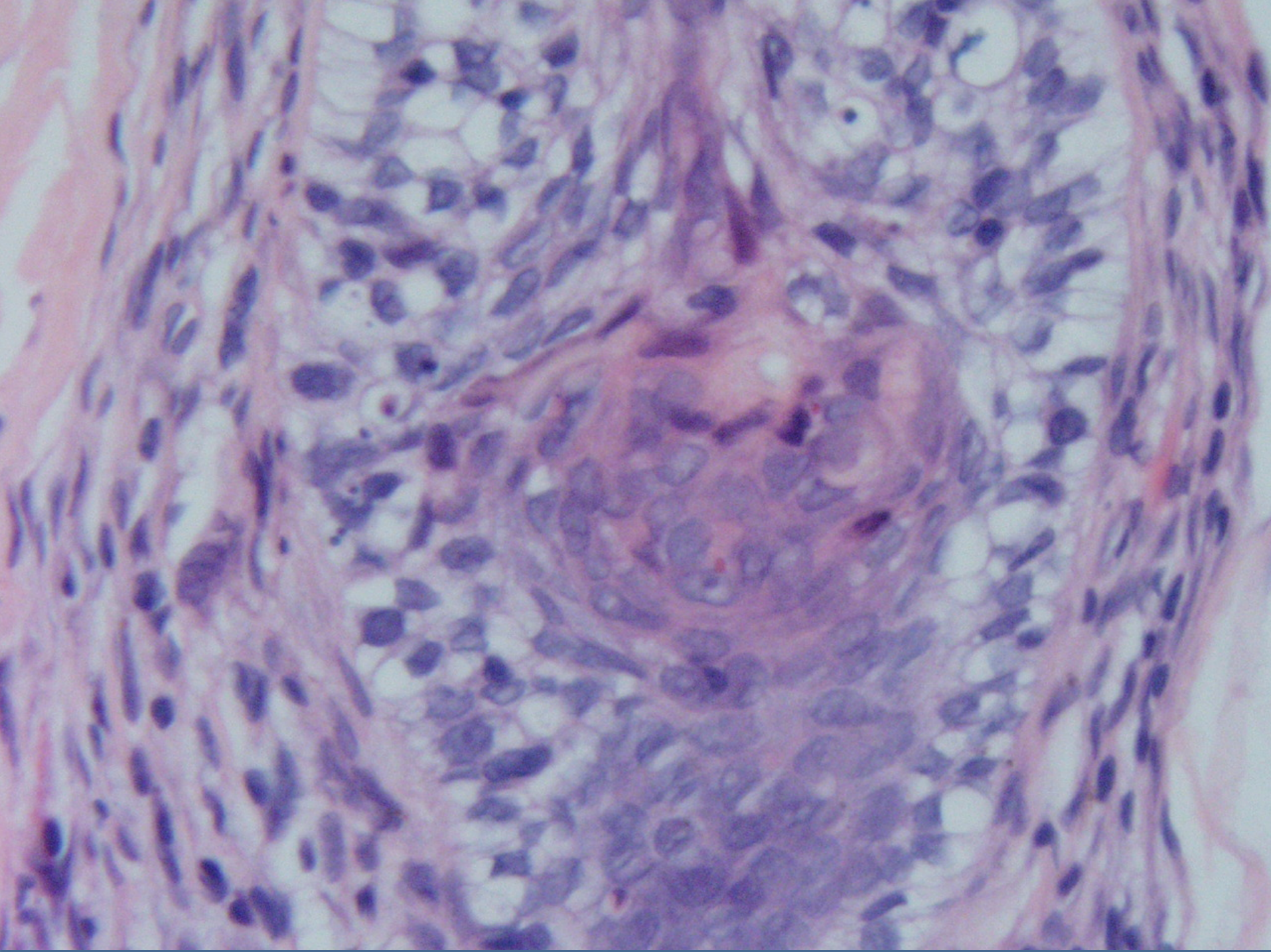












Alopecia Areata

AA-Clincial

- Usually asymptomatic
  - Some patients (14%) experience a burning sensation or pruritus
- Usually is localized
  - 80% have only a single patch
  - 12.5% have 2 patches
  - 7.7% have multiple patches
  - No correlation exists between the number of patches at onset and subsequent severity.
- Location
  - Scalp (66.8-95%)
  - Beard is affected in 28%
  - Eyebrows in 3.8%, and extremities in 1.3% of patients
  - More than one area can be affected at once.

AA-Clinical

- Localized AA
  - <50% involvement
  - Self-limited
  - Spontaneous regrowth within a few months, with or without treatment.
- Extensive AA
  - >50% involvement
  - Less common
  - AT or AU in 7% of patients
  - AA involving more than 40% hair loss is seen in 11%
  - Proportion of patients with AT appears to decrease with every decade of life
  - 30% of patients with AT, complete hair loss occurred within 6 months after onset of disease
  - Relapse rate was 90% over 5 years

AA-Disease Associations

- Atopic dermatitis
- Vitiligo
- Thyroid disease
- Collagen vascular diseases
- Diabetes mellitus
- Down syndrome
- Emotional stress and psychiatric disease: Anxiety, personality disorders, depression, and paranoid disorders
- Pernicious anemia
- Myasthenia gravis
- Ulcerative colitis
- Lichen planus
- *Candida* endocrinopathy syndrome

AA-Causes

- Precipitating factor can be found in 15.1% of patients with AA
  - Major life events, febrile illnesses, drugs, pregnancy, trauma, and many other events have been reported, but no clear conclusions
  - Most patients with AA fail to report a triggering factor preceding episodes of hair loss

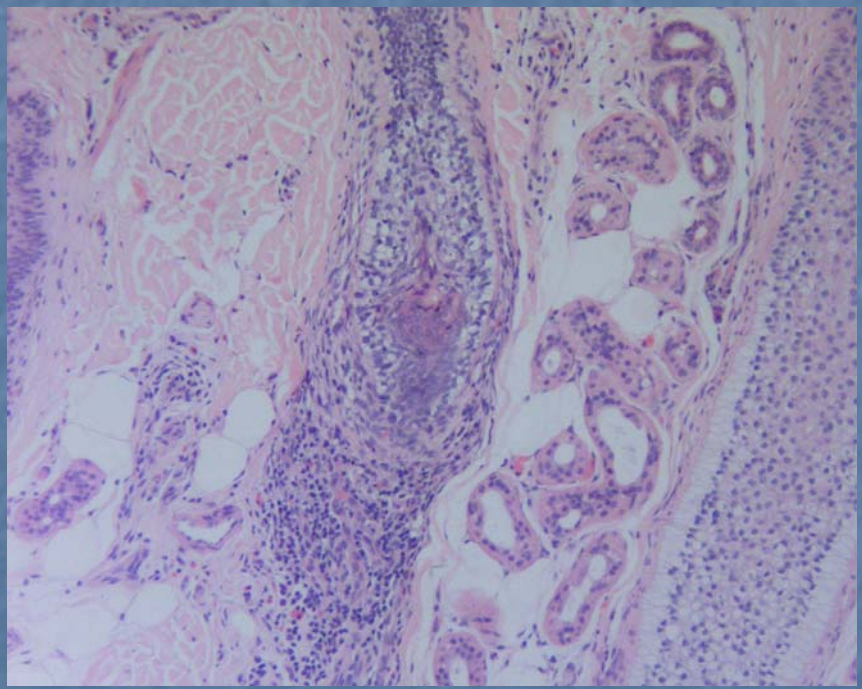
AA-Appearance

- Smooth slightly erythematous (peach color) or normal-colored alopecic patches
- Exclamation point hairs (ie, hairs tapered near proximal end) is pathognomonic-not always found.
- Positive pull test at the periphery of a plaque
  - Active disease with further hair loss
- Hair loss on other hair-bearing areas also favors the diagnosis
- Most common presentation is the appearance of 1 or many round-to-oval denuded patches
- No epidermal changes are associated with the hair loss

AA-Nails

- 6.8-49.4% of patients
  - Fingernails predominantly are affected
  - Usually with severe forms of AA
  - Pitting most common finding.
  - Other abnormalities:
    - Trachyonychia
    - Beau lines
    - Onychorrhexis
    - Onychomadesis
    - Koilonychia
    - Leukonychia
    - Red lunulae

AA-Histopathology



- Sparse peribulbar lymphocytic infiltrate, which is described as appearing similar to a swarm of bees
- Significant decrease in terminal hairs is associated with an increase in vellus hairs, with a ratio of 1.1:1 (normal is 7:1)
- Pigment incontinence in the hair bulb and follicular stellae
- Shift occurs in the anagen-telogen ratio, which is not specific
  - 73% of hairs were found to be in the anagen phase
  - 27% in the telogen phase
  - In long-standing cases of AA, the percentage of telogen phase hairs can approach 100%

AA-Treatment

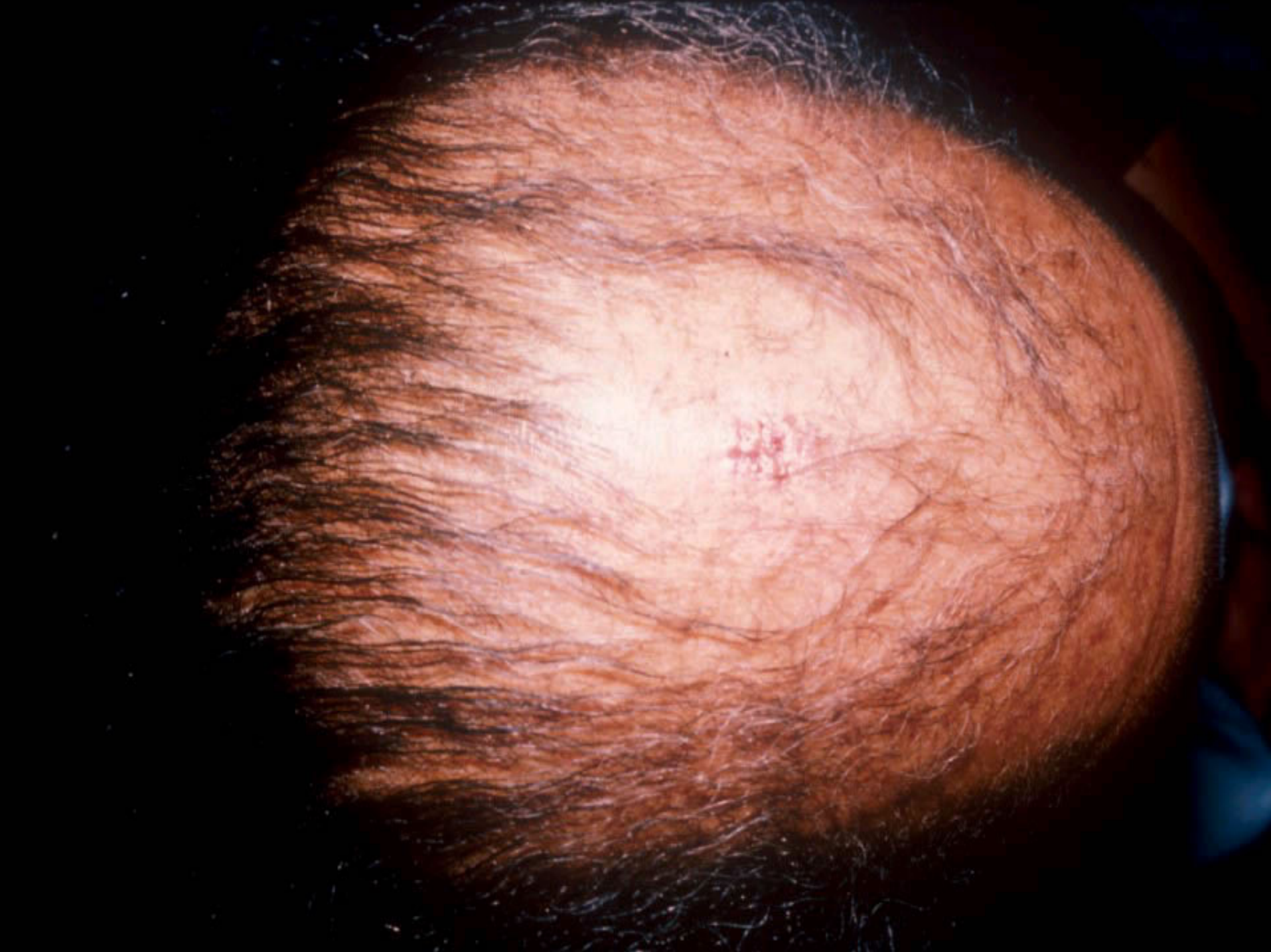
- Intralesional steroids
- Topical steroids
- Prednisone
- Topical immunotherapy
  - Squaric acid dibutylester (SADBE)
  - Diphencyprone (DPCP)
  - Dinitrochlorobenzene (DNCB)
  - Anthralin

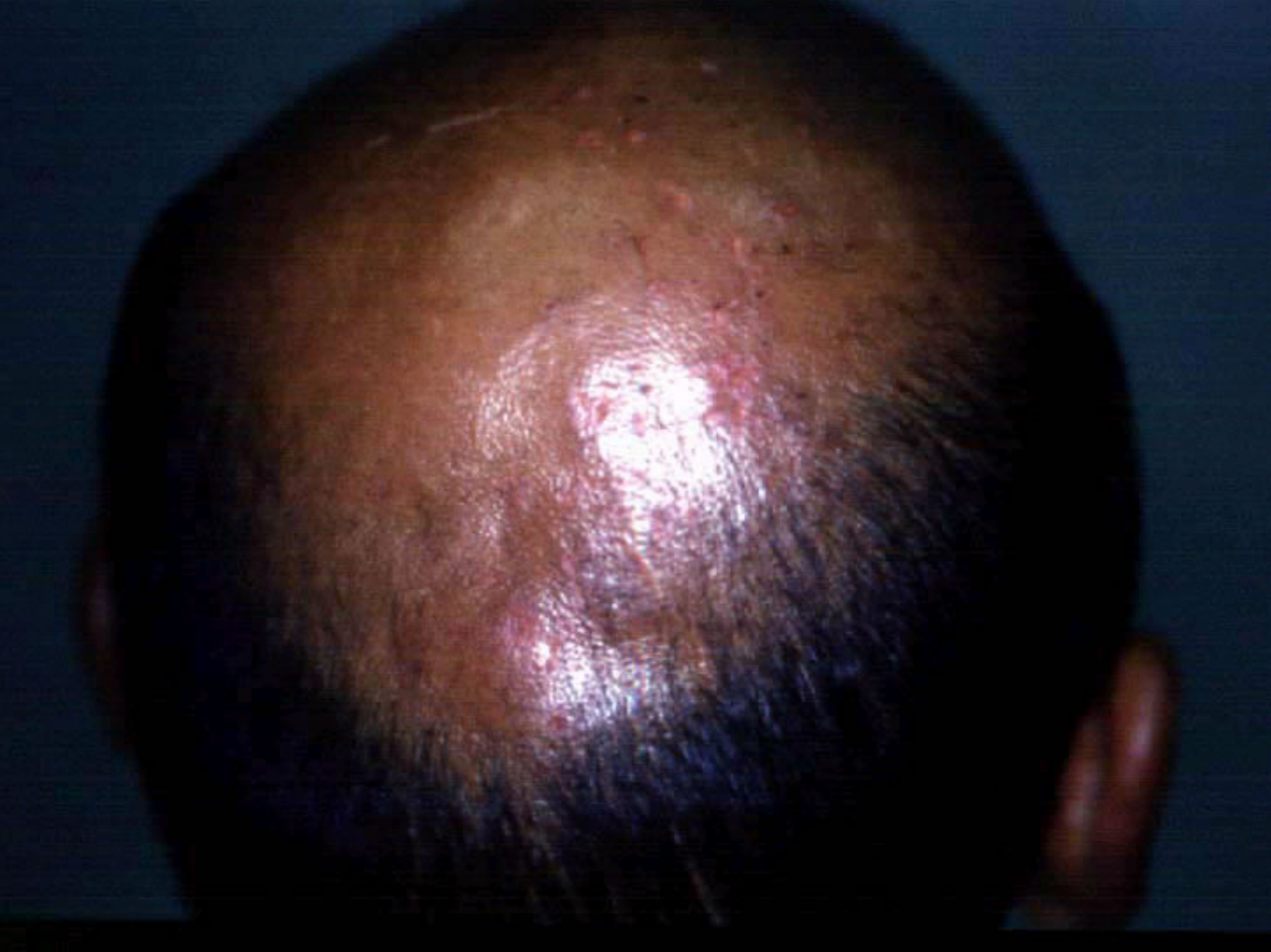
AA-Treatment

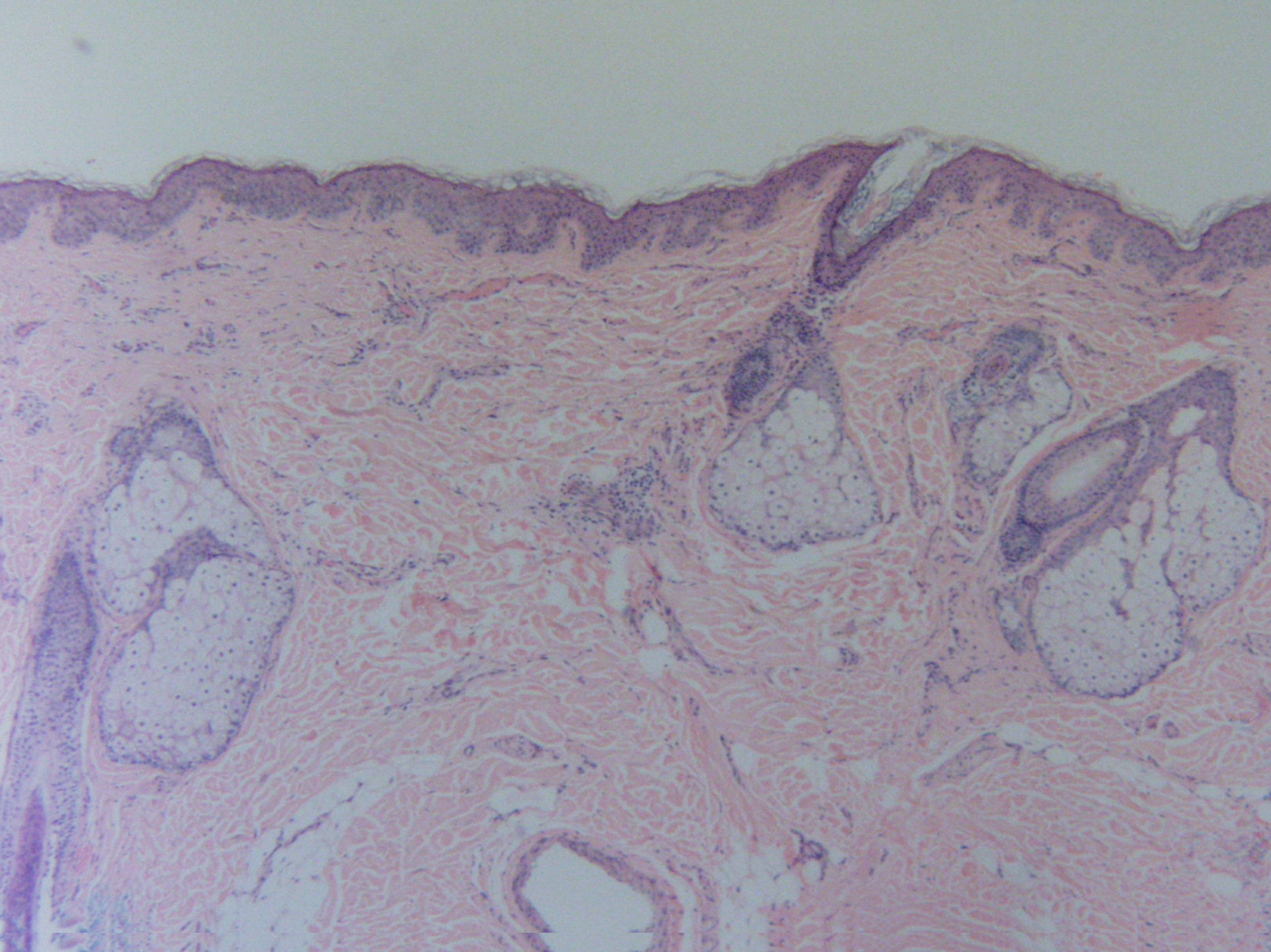
- Psoralen plus UV-A
  - Both systemic and topical PUVA therapies
- Cyclosporine, topical and oral
- Tacrolimus
- Interferon
- Dapsone
- Minoxidil

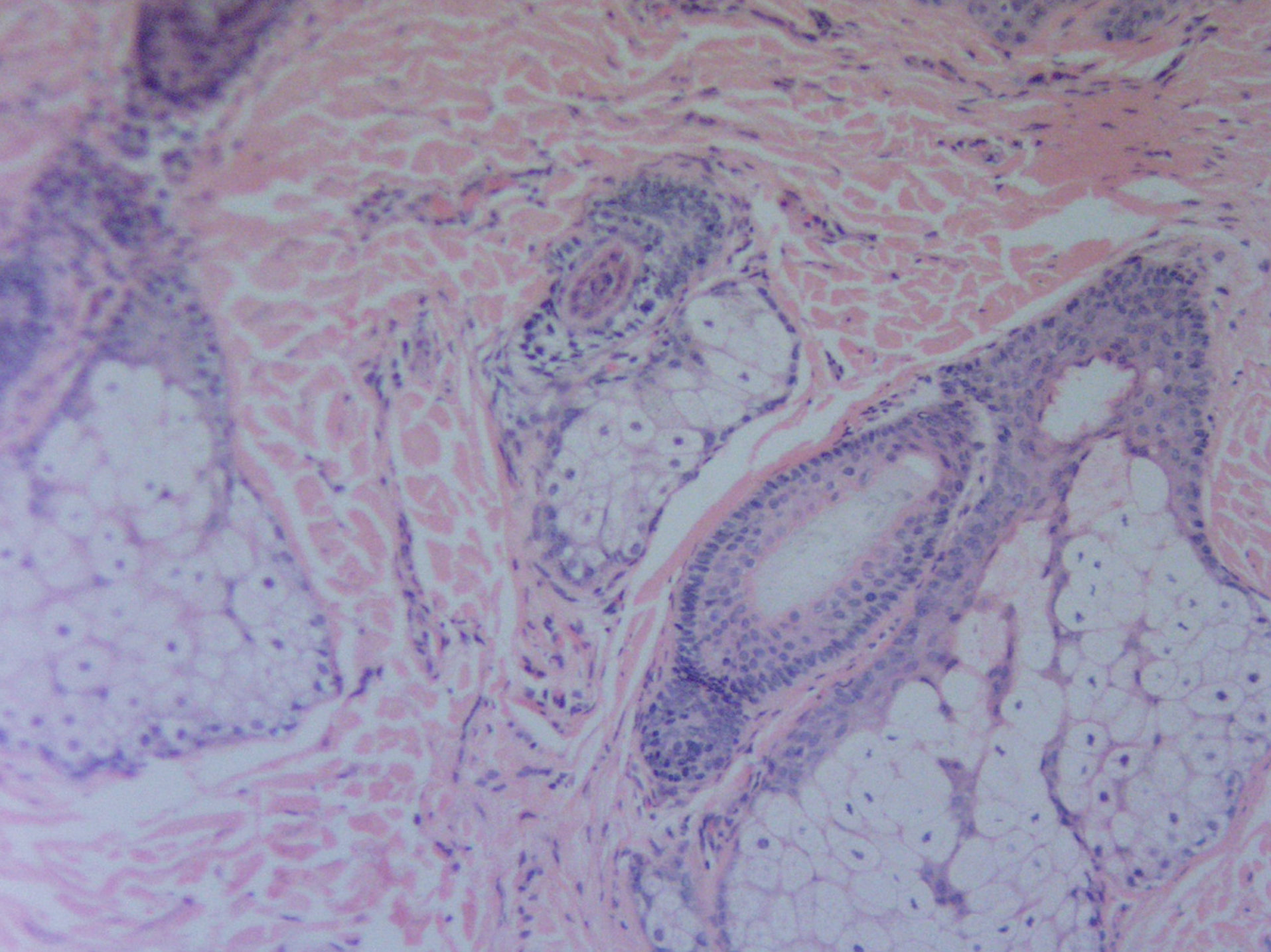
AA-Prognosis

- Unpredictable
  - Most patients have only a few focal areas of alopecia, and spontaneous regrowth usually occurs within 1 year
  - Less than 10% of patients experience extensive alopecia
  - Less than 1% have AU
- Adverse prognosis factors:
  - Extensive long-standing conditions
  - Nail abnormalities
  - Atopy
  - Onset at a young age
  - Severe forms of AA









Androgenetic Alopecia (Pattern Alopecia)

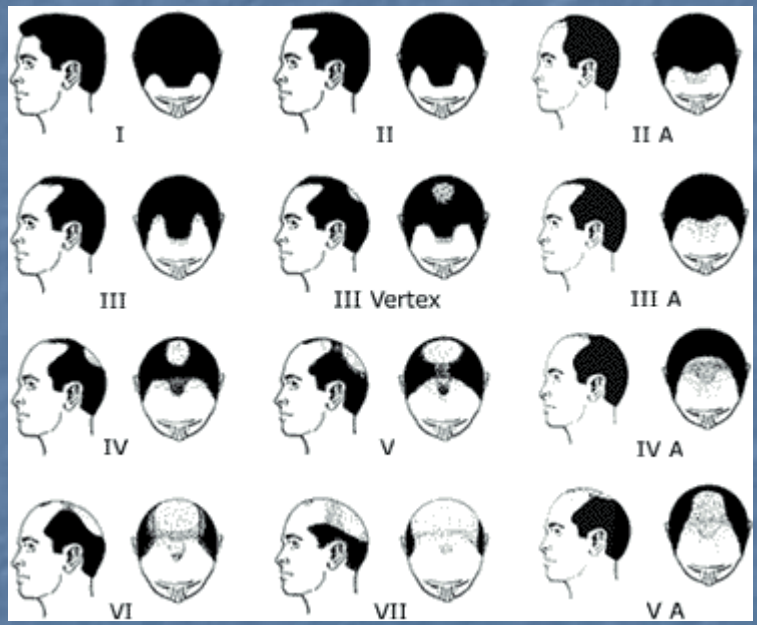
AA-Clinical

- Males>Females
- Common disorder
  - 50% of men and women >40 yrs
  - 13% of premenopausal women
  - Incidence increases following menopause
    - May affect 75% of women older than 65 years.
- Ethnicity
  - Highest in Caucasian men
  - Lowest in Native Americans and Eskimos
  - Intermediate in Asians and African-Americans

Pathogenesis

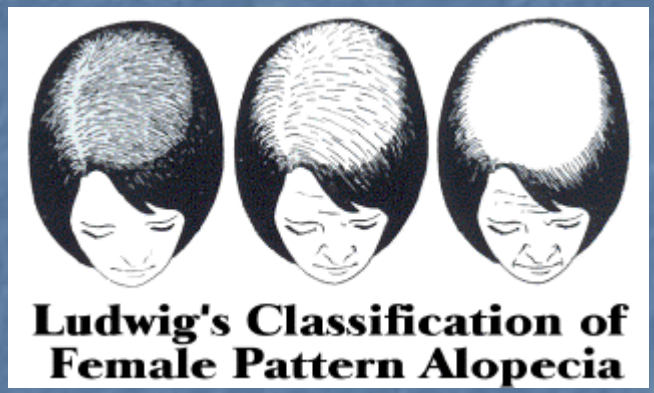
- Genetically determined
  - Dominantly inherited disorder with variable penetrance and expression
  - May be of polygenic inheritance
- Androgen is necessary for progression of the disorder
  - Not found in males castrated prior to puberty
- Progression of the disorder is stopped if postpubertal males are castrated

AA-Males



- Males evidence gradual thinning in the temporal areas producing a reshaping of the anterior hair line
  - The evolution of baldness progresses for the most part according to the Norwood/Hamilton classification of frontal and vertex thinning.

AA-Female

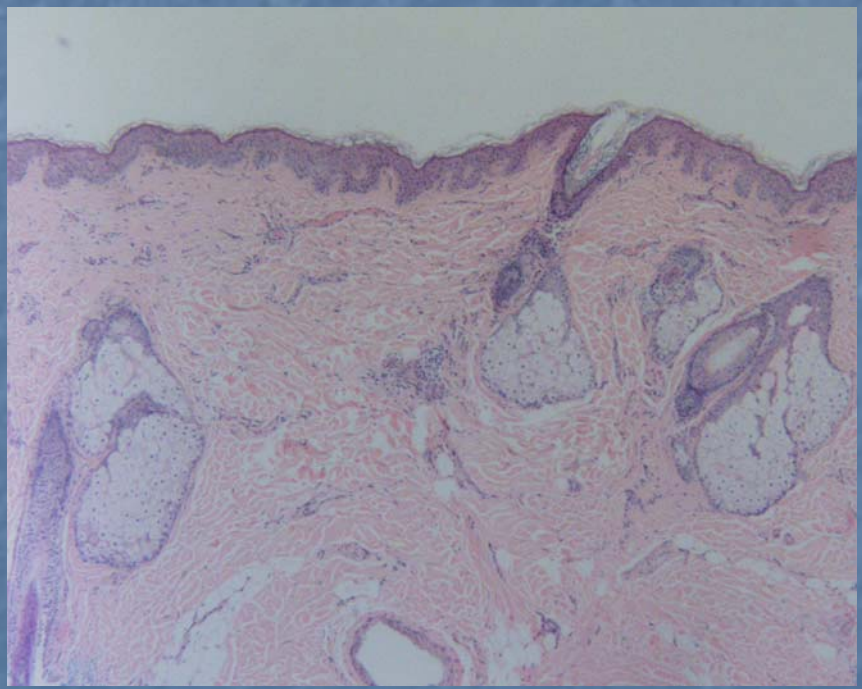


- Women, on the other hand, usually present with diffuse thinning on the crown
  - Bitemporal recession does occur in women but usually to a lesser degree than in males
  - Women in general maintain a frontal hair line

Laboratory Evaluation

- Women
  - If there is evidence of virilization, laboratory analysis of DHEA-sulfate and testosterone may be in order
  - Total testosterone alone may be adequate to screen for a virilizing tumor
  - TSH level if thyroid dysfunction suspected
- Telogen effluvium may accelerate the course of pattern alopecia
  - If telogen effluvium is present, laboratory analysis of serum iron levels, or a biopsy to note an underlying papulosquamous disorder may be indicated
  - Iron deficiency is a common and reversible cause of telogen effluvium
    - Iron, TIBC and transferrin saturation are cheap and sensitive tests for iron deficiency

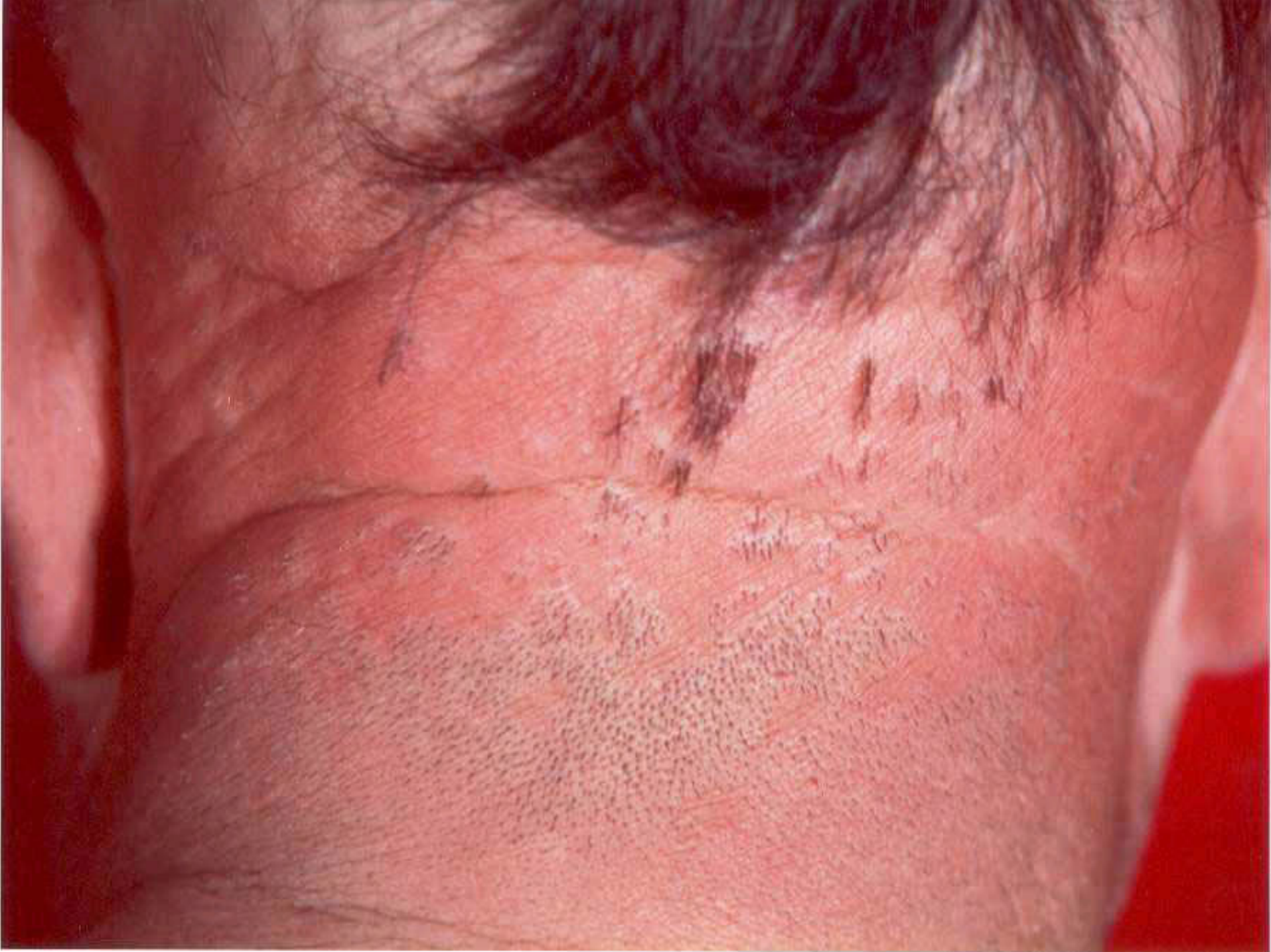
AA-Histopathology

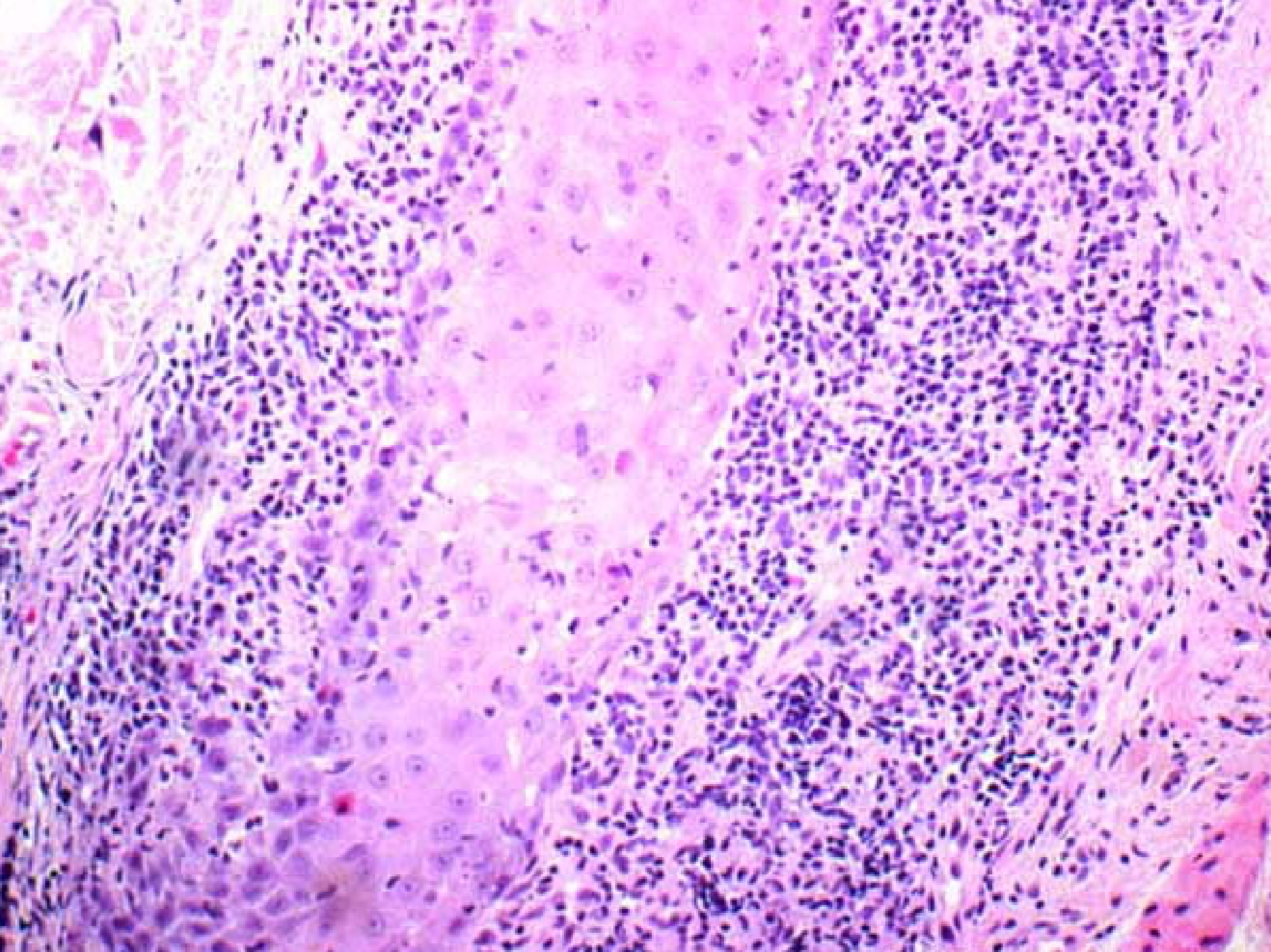


- Increase in vellus hairs is seen, and fibrous root sheaths remnants (so call "streamers") can be found below miniaturized follicles
- Mildly increased telogen-to-anagen ratio
- Rarely a superficial, perifollicular inflammatory infiltrate is noted
- In long-standing disease, connective tissue may completely replace follicular structures

Treatment

- Minoxidil
- Finasteride
- NonFDA-approved
  - Drugs that act as androgen suppressants or antagonists (eg, spironolactone and oral contraceptives)



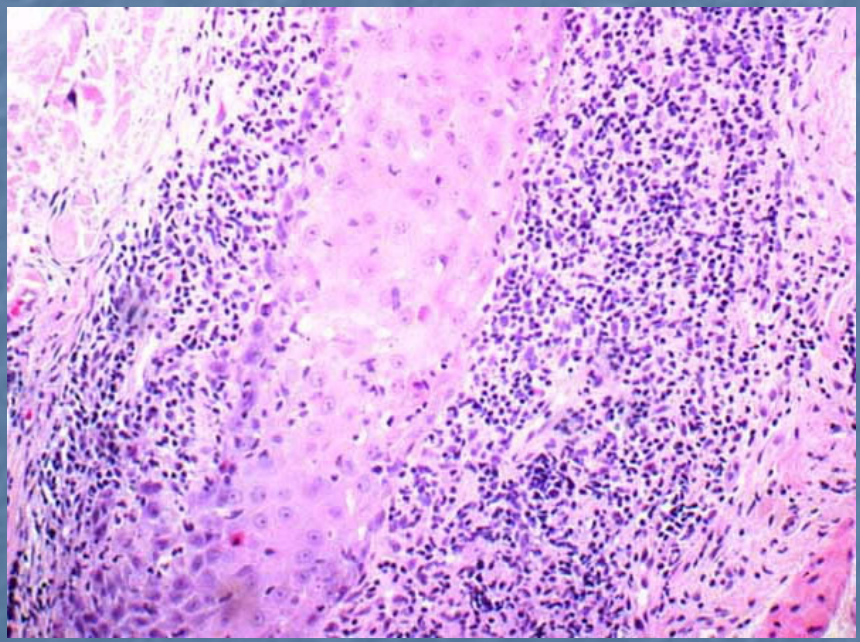


Lichen Planopilaris

Clinical Variants

- Women > Men
- Individual keratotic follicular papules
- Erythematous to violaceous plaques, some of which show follicular prominence
- Follicular papules of the scalp with concomitant or subsequent cicatricial alopecia
- Overlap common
- Graham Little-Piccardi-Lassueur syndrome-Lichen
  - Planopilaris associated with follicular keratotic lesions and alopecia

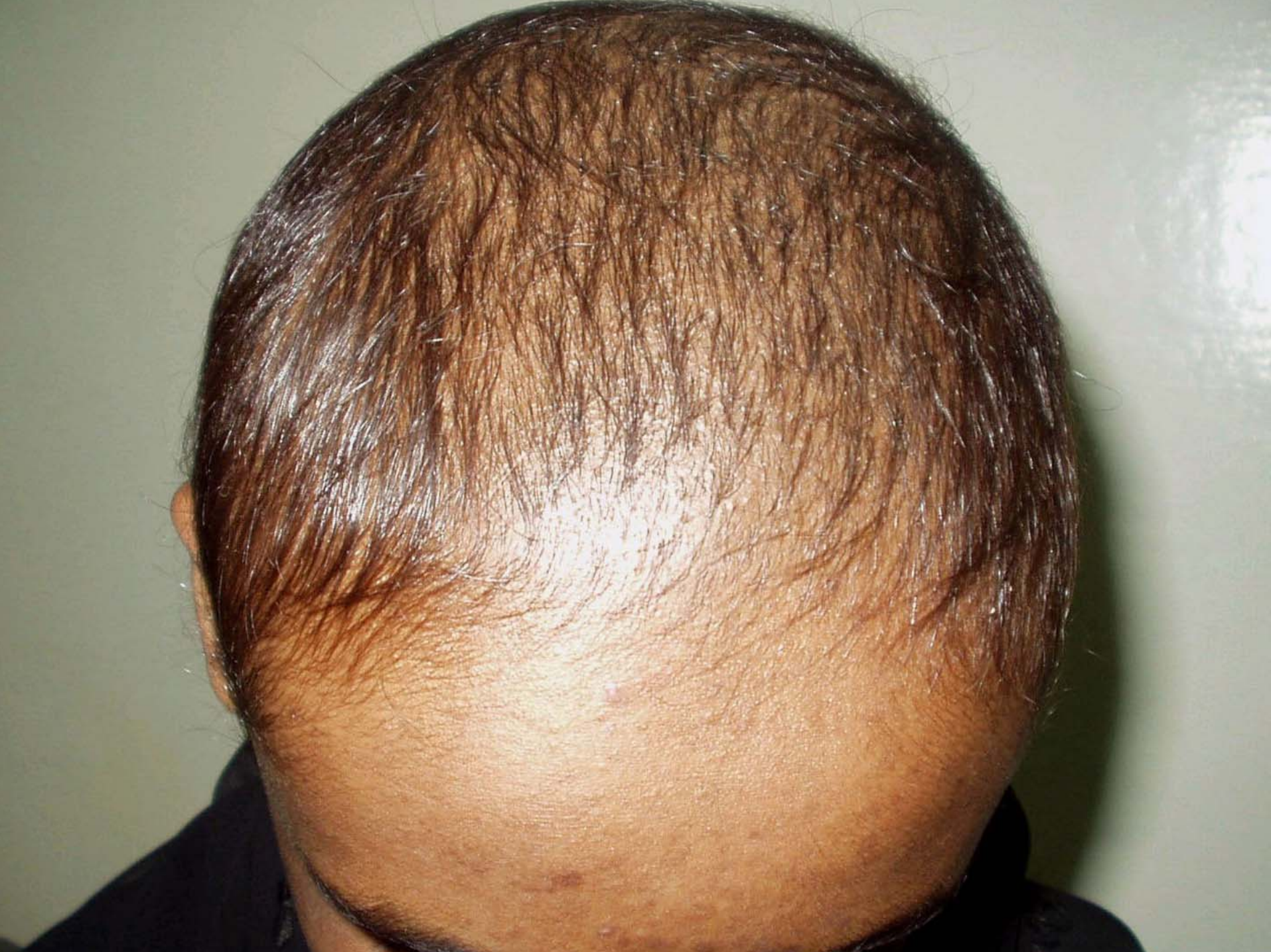
Histopathology

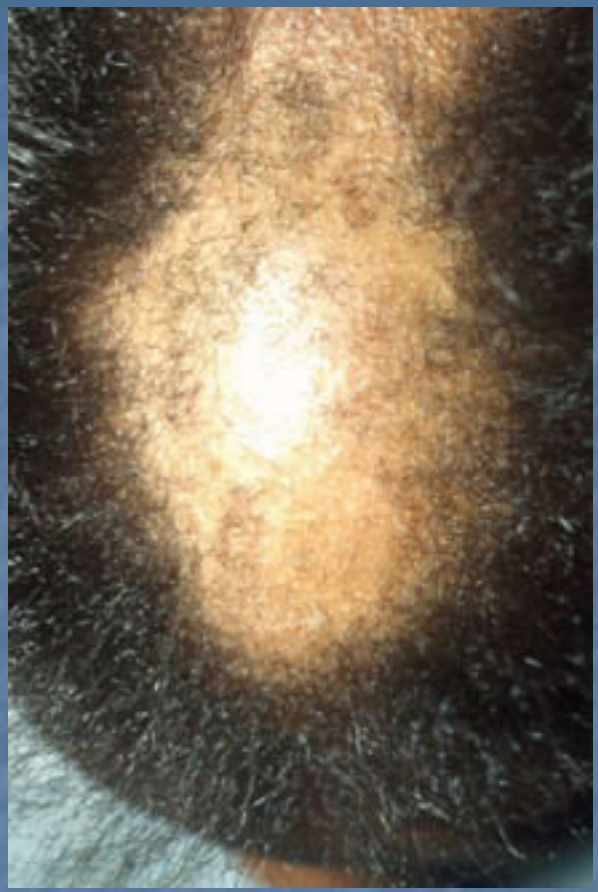


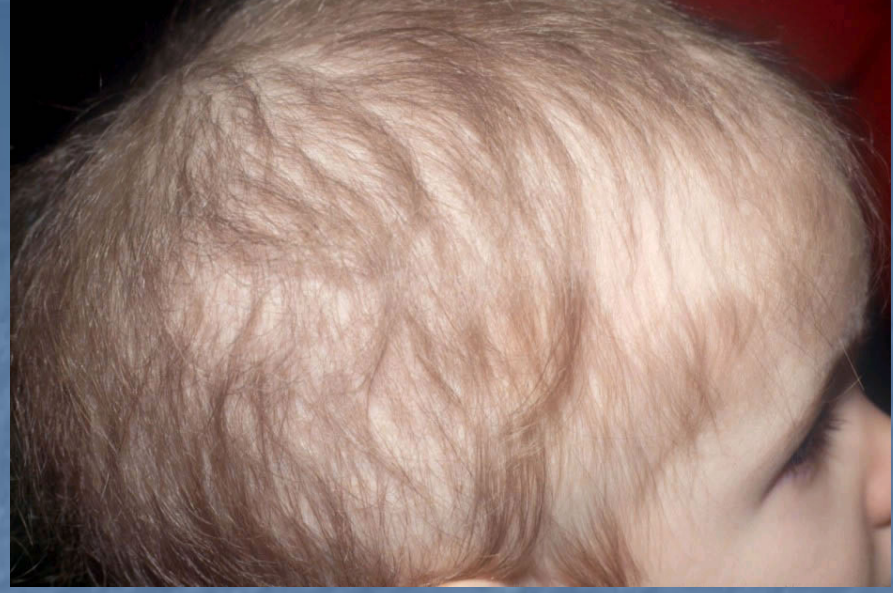
- Lichenoid inflammatory cell infiltrate confined to the follicular epithelium.
- Affects both follicular and interfollicular areas
- Lichenoid, follicular and interfollicular inflammation, associated with or followed by scarring
- Overlap common ranging from pure follicular involvement without evidence of clinical scarring to cicatricial alopecia
- DIF showed cytoid body staining with anti-IgM and anti-IgA and patchy or linear fibrinogen deposition along the basement membrane zone

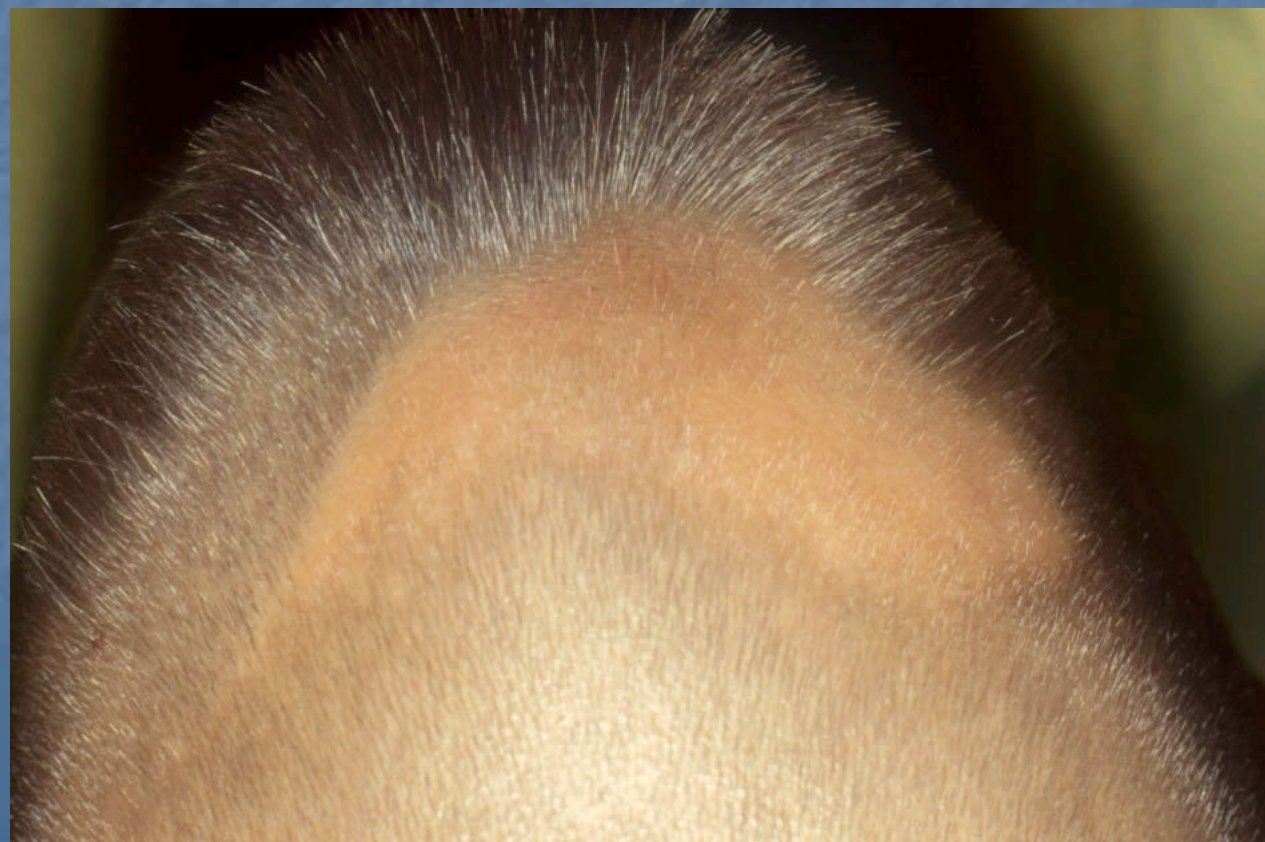
Treatment

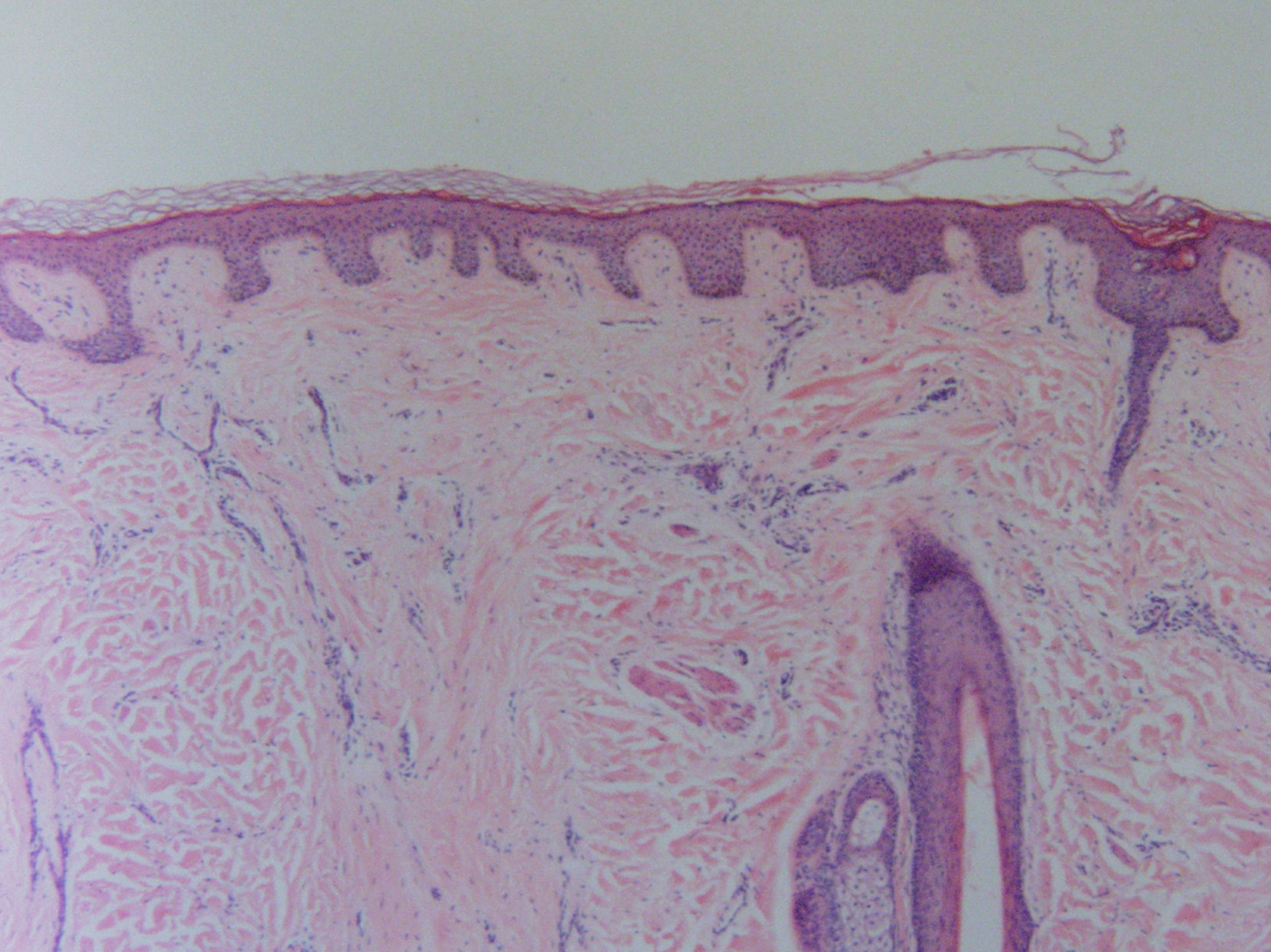
- Cyclosporin A
- Steroids
- Tacrolimus
- PUVA

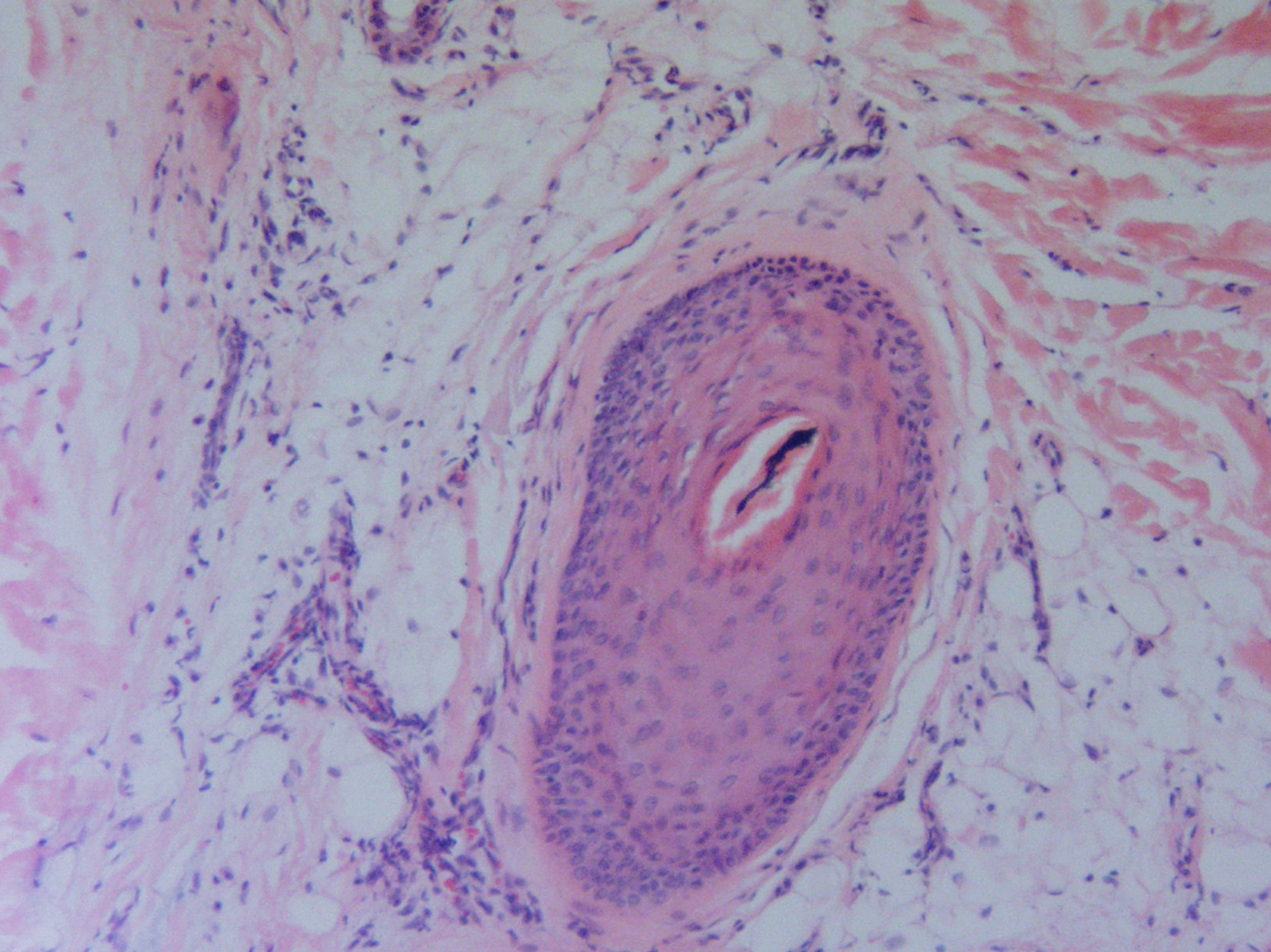


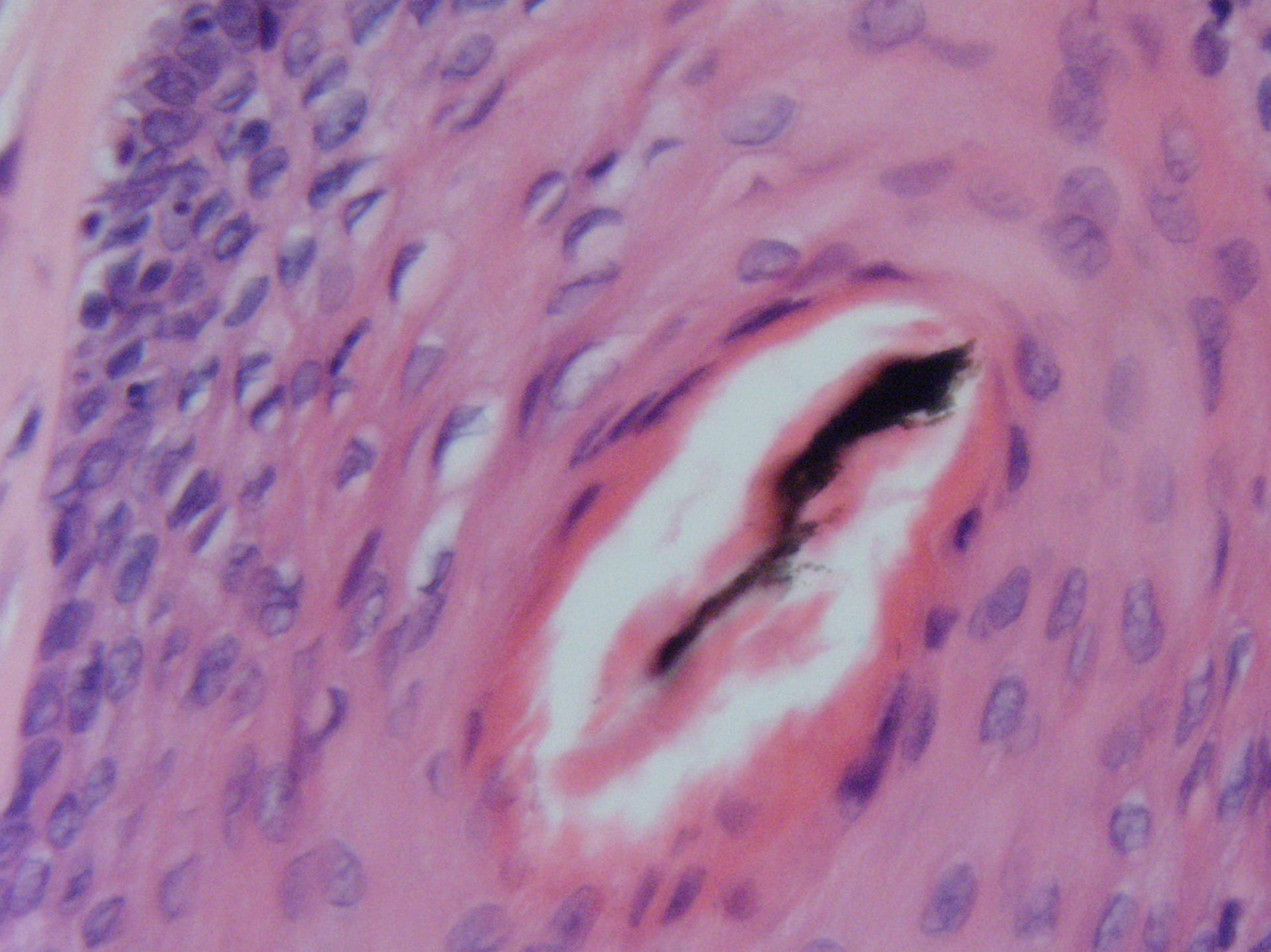












Trichotillomania/Traction Alopecia

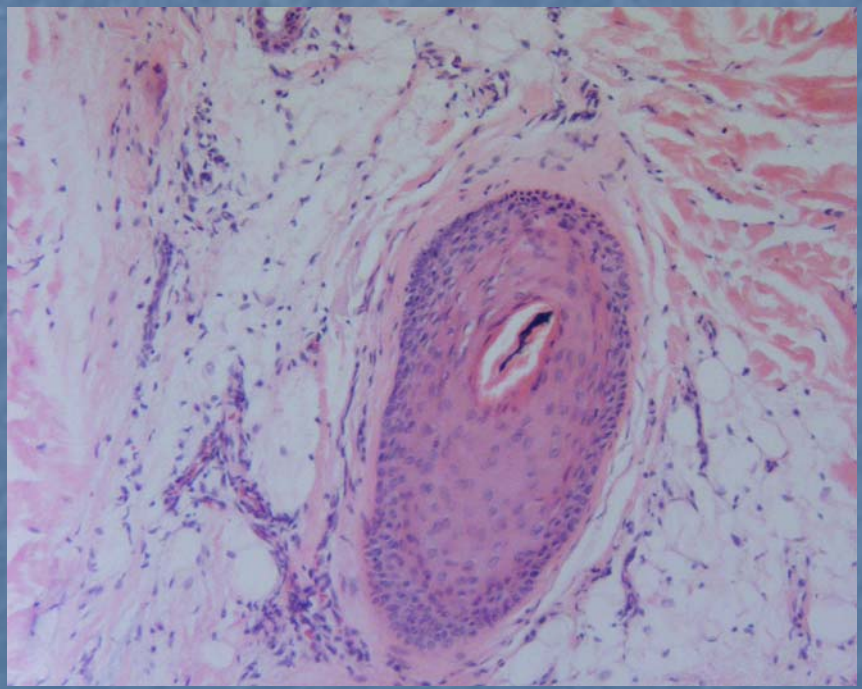
Clinical

- Geometrical shape and incomplete nonscarring alopecia of the involved area
- Single or multiple
  - Vary from only a few square centimeters to an extensive involvement of the scalp, sparing only marginal areas
  - Entire involvement possible
- Various combinations of the following:
  - Newly growing short hairs with tapered ends
  - Broken short hairs
  - Vellus or indeterminate hairs
  - Comedolike black dots
  - Empty follicular orifices.
- Eyebrows and eyelashes, may be involved
- Extremely short fingernails (from nail biting) often accompany trichotillomania in children

Causes

- Trichotillomania suggests the act of plucking (*tillein* is Greek for "to pluck, pull out"), actual plucking seems to be a minor component
- Types of manipulations
  - Rubbing, twisting, breaking, pulling (not forcible plucking), and plucking
  - If the force of pulling (versus plucking) induces premature entry of the follicles into the catagen phase, this would subsequently lead to increased hair shedding
- To understand trichotillomania, understanding both the biology of hair and the patient's psychologic state are needed

Histopathology



- Empty anagen follicles, increased numbers of noninflamed catagen follicles, and pigment casts in hair canals
- Trichomalacia (incompletely keratinized, distorted, and pigmented hair shafts)
  - Once was regarded specific for trichotillomania, is found in less than one half of the total cases and also is seen in acute alopecia areata.
- DDX:
  Increased numbers of catagen hairs and pigment casts within hair canals may be seen in alopecia areata and syphilis and in trichotillomania

DDX-Traction Alopecia

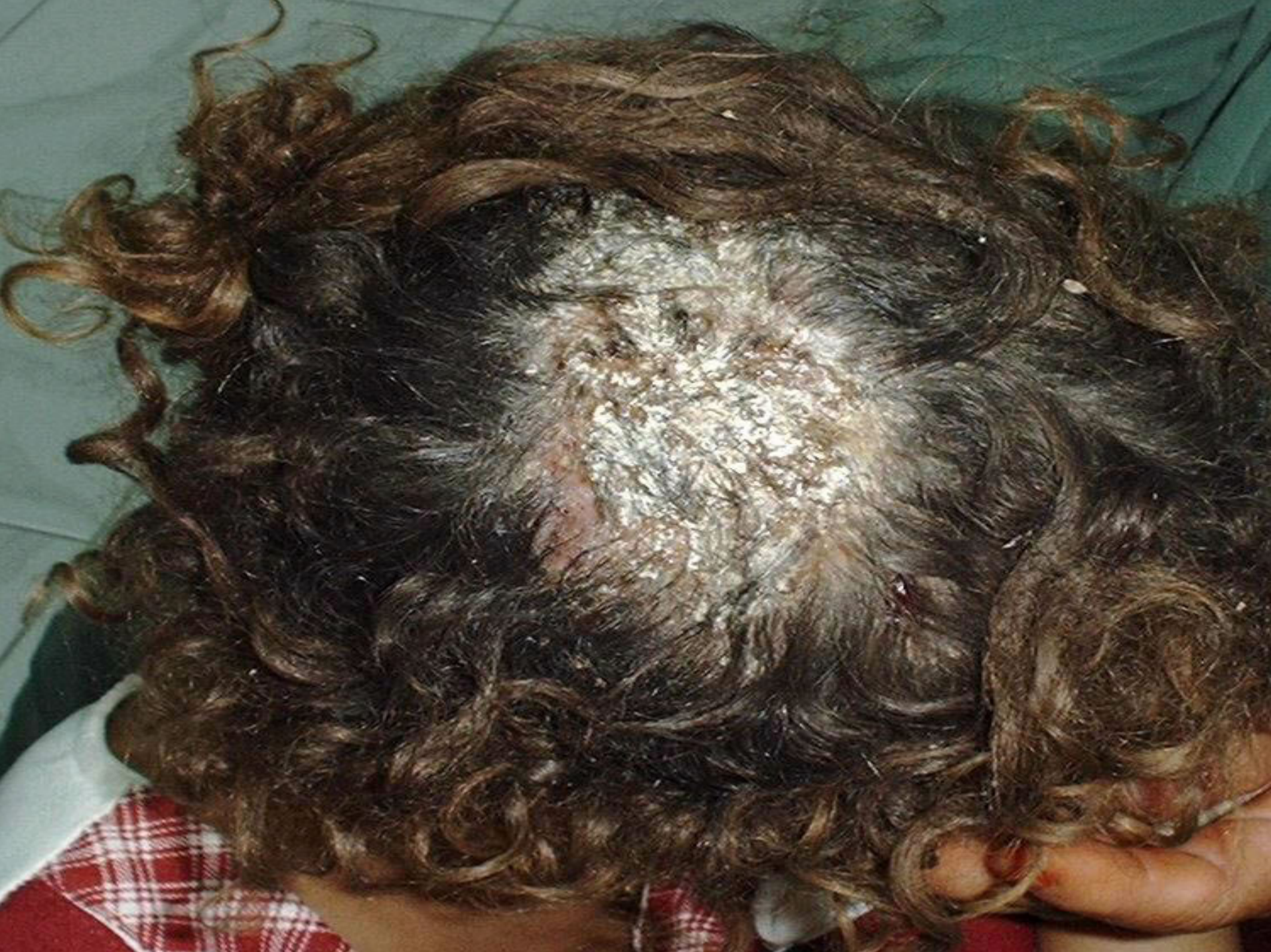
- Early changes
  - Lymphocytes surround a lichenoid perifolliculitis with infundibula
- Later changes
  - Zone of fibroplasia separates this infiltrate
- Fully developed
  - Mild lymphocytic perivascular infiltrate, a markedly thinned lower infundibulum, and an isthmus surrounded by a band of fibroplasia
  - Foreign body granuloma may be evident
  - The late process has a reduced number of hair follicles and thickened fibrous bands in much of the reticular dermis that extend into subcutaneous fat

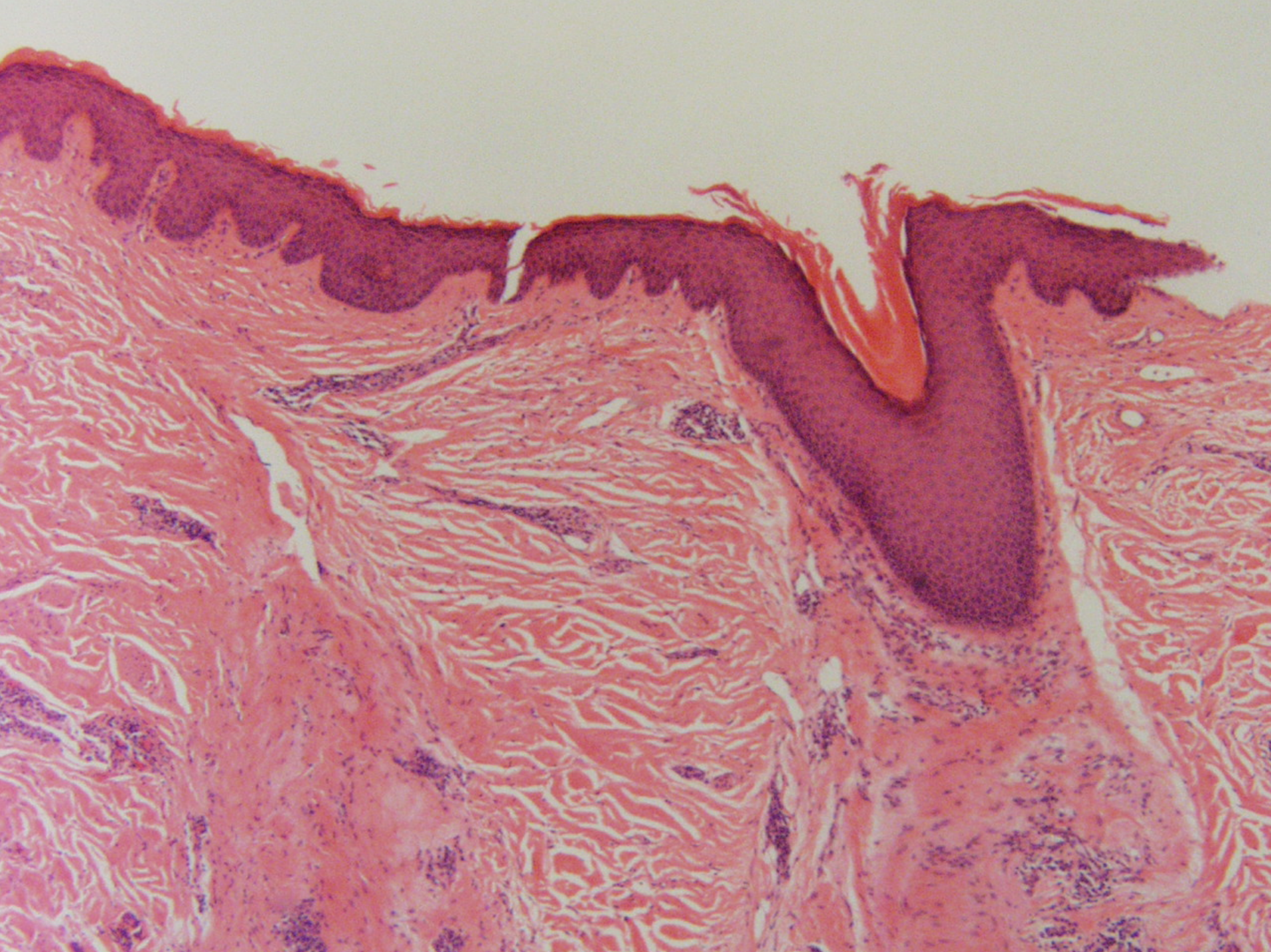
Treatment

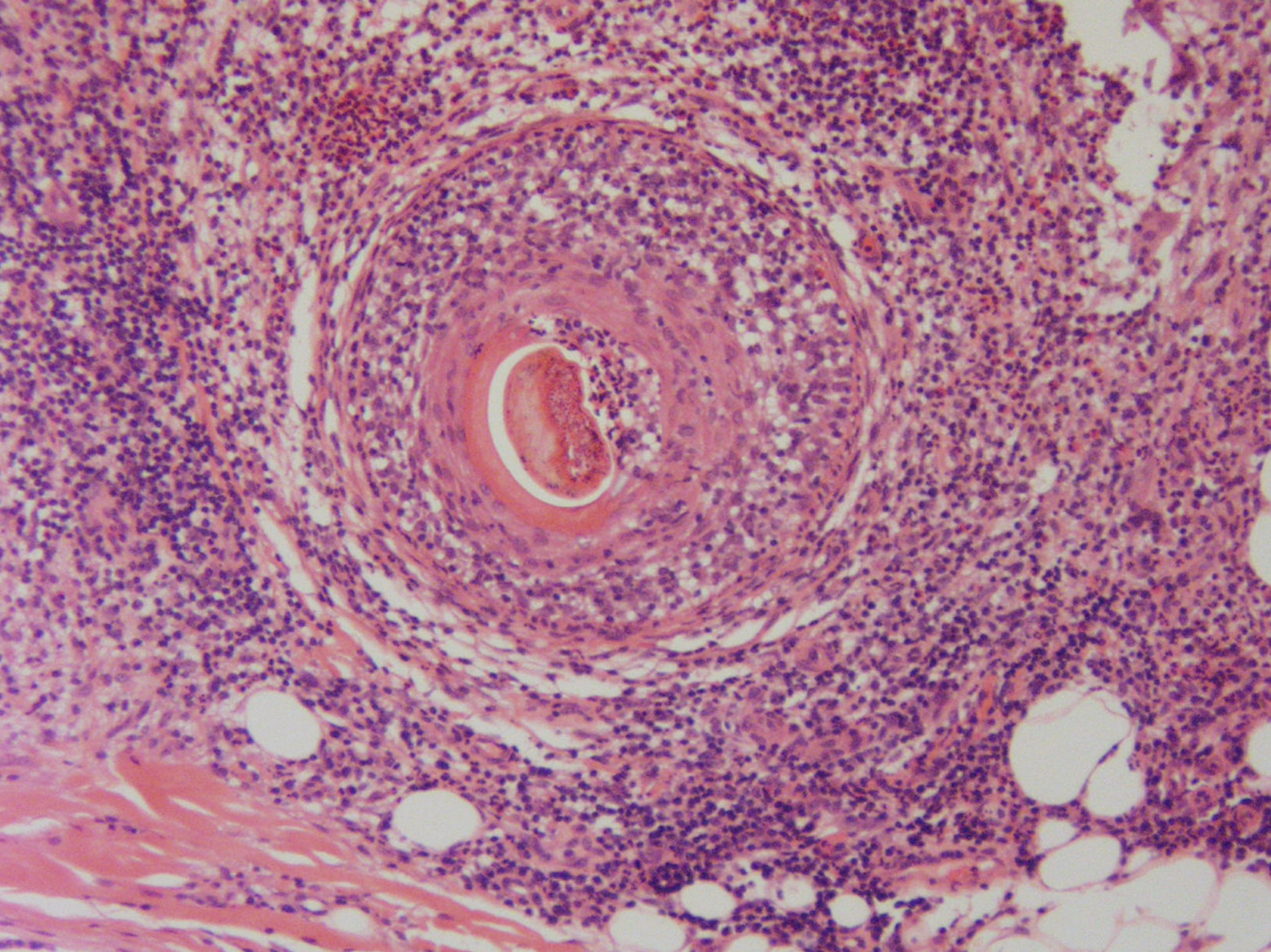
- Supportive care by the dermatologist may be sufficient
- Shaving or clipping hairs close to the scalp may be helpful to stop the behavior and to assure the parents of the nature of the alopecia
- Adult groups
  - Psychiatric clinics
  - Clomipramine causes short-term improvement in adult patients

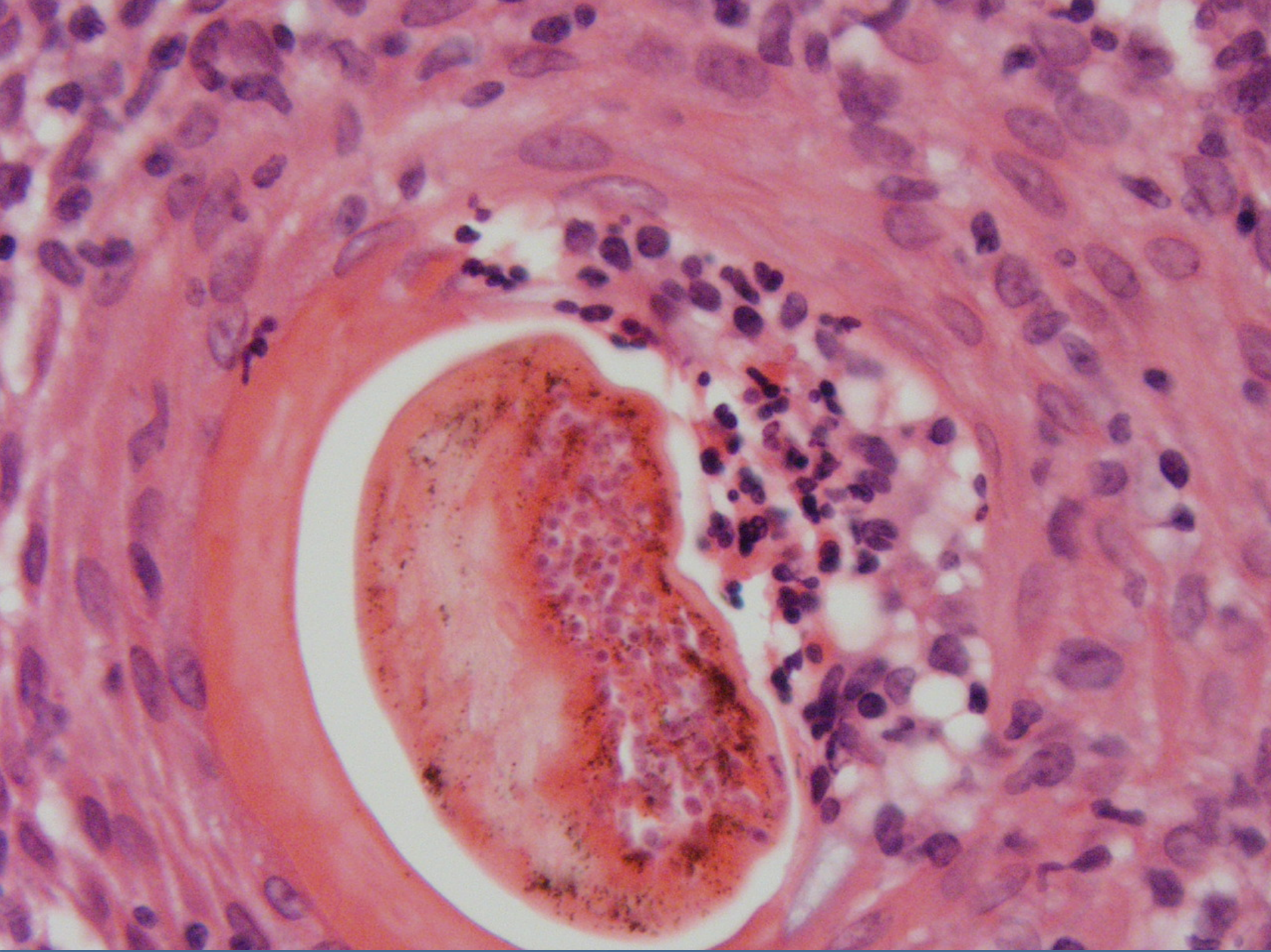
Prognosis

- In very young children, the prognosis is excellent.
- In late childhood and adolescence, the prognosis is usually good but is more guarded than in young children. The alopecia quite often recurs after a variable time.
- In adult patients, the prognosis is poor, and permanent recovery is uncommon.









Tinea Capitis

Clinical

- Childhood disease
  - 92.5% of dermatophytoses in children younger than 10 years
  - Most common in children younger than 10 years
  - Peak age range 3-7 years
- Rare in adults
- Widespread in some urban areas in North America, Central America, and South America

Clinical

- Early
  - Small erythematous papule around a hair shaft on the scalp, eyebrows, or eyelashes.
- Later
  - Red papule becomes paler and scaly, and the hairs appear discolored, lusterless, and brittle
  - Break off a few millimeters above the scalp skin surface
  - The lesion spreads, forming numerous papules in a typical ring form
  - Ring-formed lesions may coalesce with other infected areas
  - Pruritus usually is minimal but may be intense at times.
  - Alopecia is common in infected areas
  - Inflammation may be mild or severe
    - Deep boggy red areas characterized by a severe acute inflammatory infiltrate with pustule formation are termed kerions or kerion celsi

Favus

- Favus (also termed tinea favosa) is a severe form of tinea capitis.
  - Favus is a chronic infection and is caused most commonly by *T schoenleinii* and, occasionally, by *Trichophyton violaceum* or *Microsporum gypsum*.
  - Scalp lesions are characterized by the presence of yellow cup-shaped crusts termed scutula, which surround the infected hair follicles.
  - Favus is seen predominantly in Africa, the Mediterranean, and the Middle East and, rarely, in North America and South America, usually in descendants of immigrants from endemic areas.
  - Favus usually is acquired early in life and has a tendency to cluster in families
  - Infected hairs appear yellow

Epidemiology

- United States
  - *Trichophyton tonsurans* has replaced *M audouinii* and *M canis* as the most common cause of tinea capitis
  - *T tonsurans* most common cause of the disease in Canada, Mexico, and Central America.
- Europe
  - *M audouinii* was the classic causative agent in Europe and America
  - *M audouinii* and *M canis* remain prevalent in most parts of Europe
  - *T violaceum* also is common in Romania, Italy, Portugal, Spain, and the former USSR
- Africa
  - *T violaceum*, *T schoenleinii*, and *M canis*
- Asia
  - *T violaceum* and *M canis*
  - *Microsporum ferrugineum* most common in Asia

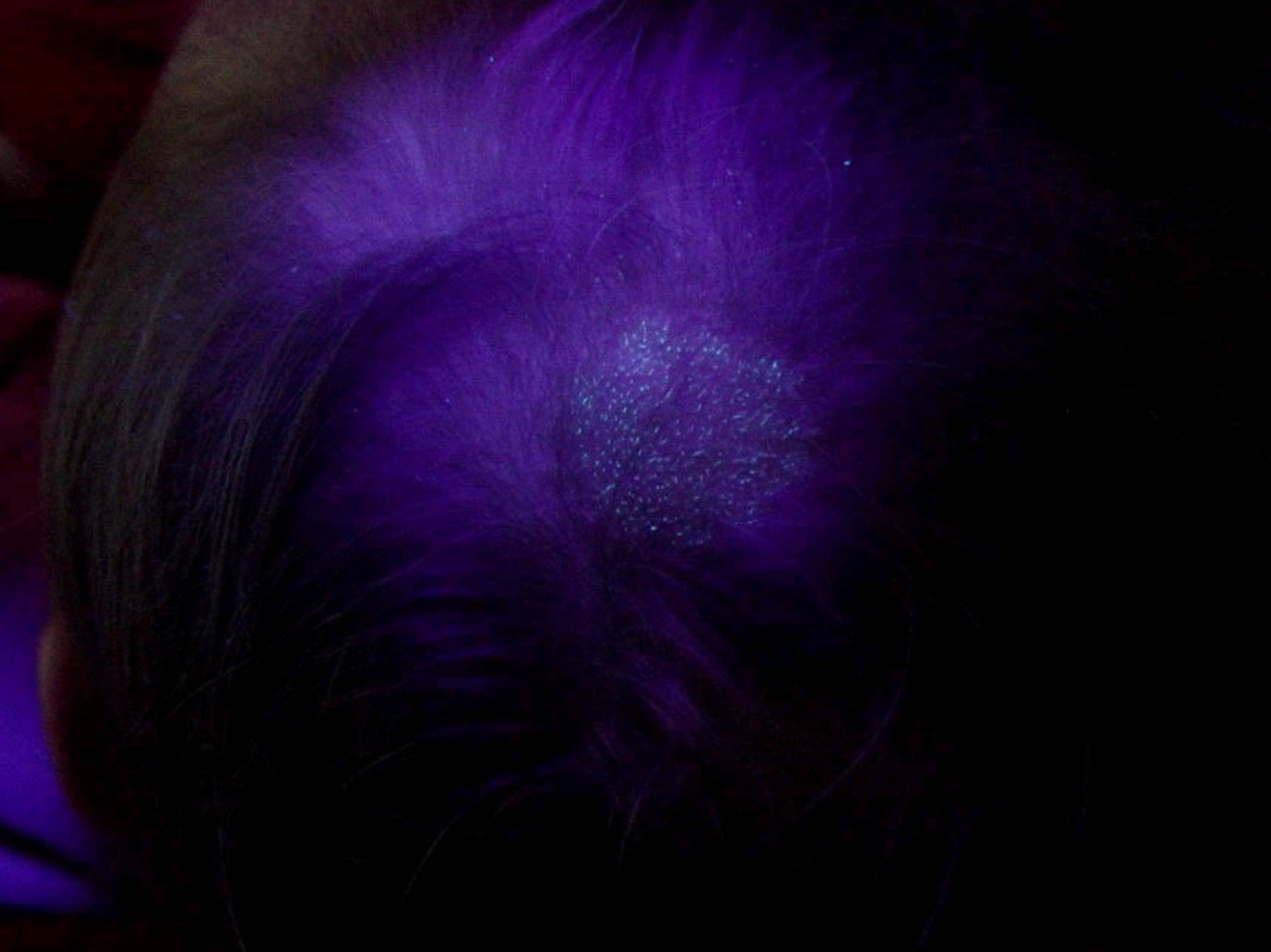
NOTE: Trichophyton rubrum, most common dermatophyte isolated worldwide, is not a common cause of tinea capitis.

Epidemiology

- *Microsporum audouinii*
  - Boys 5 times higher than in girls
  - Reverse is true after puberty
    - Result of increased exposure to infected children by women and to hormonal factors
- *Microsporum canis*
  - Infection rate usually is higher in males
- *Trichophyton*
  - Girls and boys are affected equally
  - Adults, women are infected more

Pathogenesis

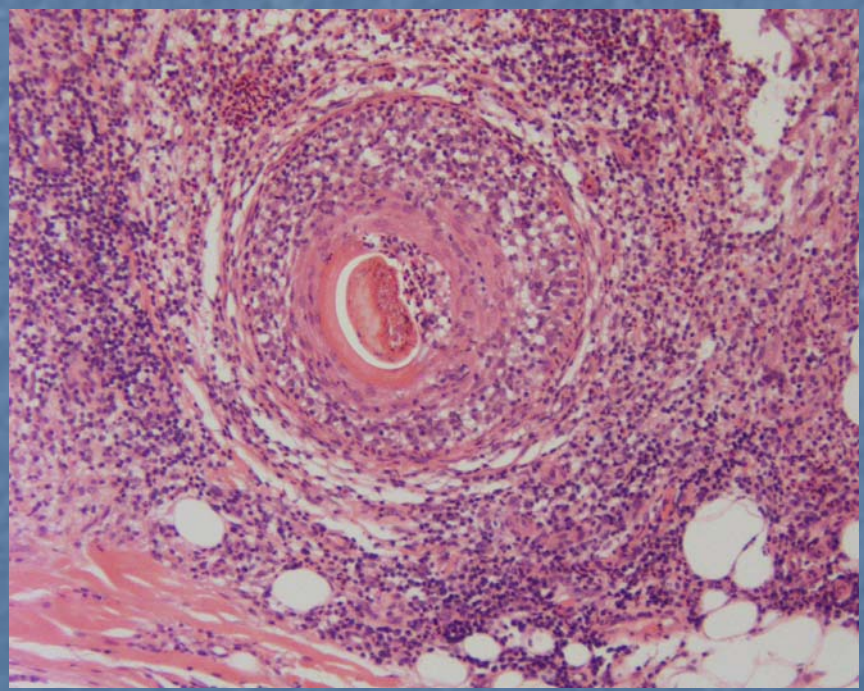
- Endothrix (inside the hair shaft) vs. ectothrix (extending outside the hair shaft)
- Endothrix infection:
  - *T tonsurans*, characterized by chains of large spores
    - Suppuration and kerion formation commonly are associated with *T tonsurans* infection.
  - *T schoenleinii*, characterized by hyphae with air spaces
- Ectothrix infection, fragmentation of the mycelium into spores occurs just beneath the cuticle with destruction of the cuticle
  - *Trichophyton verrucosum*
  - *T mentagrophytes*
  - *Microsporum* species



Laboratory

- Wood's Lamp
  - Positive for ectothrix infection
- KOH prep
  - Microscopic examination small-spore or large-spore ectothrix or endothrix
- Culture
  - Precise identification of the species
  - Sabouraud agar containing antibiotics (penicillin/streptomycin or choramphenicol) and cycloheximide (Acti-dione)
  - Most dermatophytes can be identified within 2 weeks
    - *T verrucosum* grows best at 37ºC

Histopathology

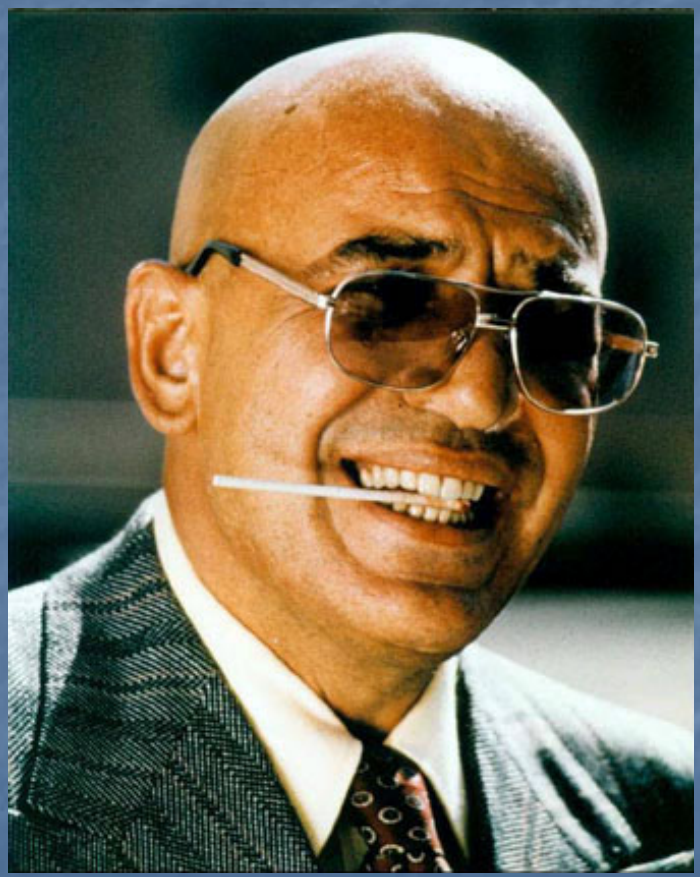


- Suppurative folliculitis may be present.
- Hyphae extend down the hair follicle, and may invade shaft and cuticle
- Kerion
  - Pronounced inflammatory tissue reaction with follicular pustule formation surrounding hair follicles is
- Endothrix infection:
  - Spheric–to–box-like spores are found within the hair shaft (T *tonsurans* or *T violaceum)*
- Ectothrix infection:
  - Organisms form a sheath around the hair shaft
  - In contrast to endothrix infection, destruction of the cuticle by hyphae and spores occurs

Treatment

- Oral griseofulvin
- Topical treatment usually ineffective
- Oral Ketoconazole, itraconazole, terbinafine, and fluconazole effective
- Selenium sulfide shampoo
  - May reduce the risk of spreading the infection early in the course of therapy by reducing the number of viable spores that are shed

Questions



- For three days after death hair and fingernails continue to grow but phone calls taper off.

Johnny Carson